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Nothnagel's Practice

TUBERCULOSIS

AND

ACUTE GENERAL MILIARY TUBERCULOSIS

BY

PROF. DR. G. CORNET
of Berlin

EDITED, WITH ADDITIONS

BY

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AUTHORIZED TRANSLATION FROM THE GERMAN, UNDER THE
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PREFACE.

THE excellence of the series of monographs issued under the editorship of Professor Nothnagel has been recognized by all who are sufficiently familiar with German to read these works, and the series has found a not inconsiderable proportion of its distribution in this and other English-speaking countries. I have so often heard regret expressed by those whose lack of familiarity with German kept these works beyond their reach, that I was glad of the opportunity to assist in the bringing out of an English edition. It was especially gratifying to find that the prominent specialists who were invited to co-operate by editing separate volumes were as interested as myself in the matter of publication of an English edition. These editors have been requested to make such additions to the original articles as seem necessary to them to bring the articles fully up to date and at the same time to adapt them thoroughly to the American or English reader. The names of the editors alone suffice to assure the profession that in the additions there will be preserved the same high standard of excellence that has been so conspicuous a feature in the original German articles.

In all cases the German author has been consulted with regard to the publication of this edition of his work, and has given specific consent. In one case only it was unfortunately necessary to substitute for the translation of the German article an entirely new one by an American author, on account of a previous arrangement of the German author to issue a translation of his article separately from this series. With this exception the Nothnagel series will be presented intact.

ALFRED STENGEL.

EDITOR'S PREFACE.

The American edition of Professor Cornet's exhaustive work appears at a time when the subject of tuberculosis has a peculiar claim upon the attention of mankind. Within a few years, both professional and general public interest in the disease has taken enormous strides.

In almost every civilized community societies for the prevention of tuberculosis are being organized, and these are composed not only of physicians but of laymen, while governments themselves are taking an active part in the movement, and special laboratories are being founded for the study of the disease, maintained by private and public munificence. Under these circumstances, and at this time, the work of Professor Cornet deserves to be made easily available to students of all nationalities, for there is no other treatise which gives an equally clear and comprehensive view of this subject.

On this account, and because the work is so complete and so logically arranged, it has seemed best to make no changes in the original, and to limit additions to such topics as have developed or become more prominent since the appearance of the work in German, such as the question of the relation of human to bovine tuberculosis, and the subject of artificial immunity, and many others of less importance. These additions, moreover, have been made as brief as possible, and have been introduced in such a way as to interfere as little as might be with the continuity of the original work. The editor has carefully refrained from discussing or criticizing any views held by the author, believing that he would best serve the profession by presenting the work of Professor Cornet as it was written.

The growing importance of the chemical side of tuberculosis, and its bearing upon the problems of immunity, together with the large number of facts that have been accumulated in the past four years, have seemed to warrant a broader treatment of this part of the subject; and the editor has been fortunate in securing from Dr. E. R. Baldwin, of Saranac Lake, a special chapter upon the chemistry of the tubercle bacillus.

The editor desires to acknowledge his indebtedness to the editor in chief, Professor Stengel, for helpful suggestions; to the secretary of the tuberculosis committee of the Charity Organization Society of New York for the list of the principal sanatoria of the United States and Canada; and to Drs. L. F. Frissell, John Howland, and E. L. Trudeau, Jr., for aid in the preparation of the manuscript and in the reading of the proofs.

WALTER B. JAMES.

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TUBERCULOSIS.

TUBERCULOSIS.

INTRODUCTION.

SIGNIFICANCE OF TUBERCULOSIS.

If one judges of the importance of a disease according to its distribution, and according to the degree in which it menaces health and induces death prematurely, tuberculosis assumes the first rank in human pathology. In its most frequent manifestation, pulmonary consumption, it has been known as far back as the memory of man extends, and has unceasingly decimated the race for hundreds and thousands of years. Since the conception of the number of diseases comprehended under the terms tuberculosis and phthisis has been at times narrower, at times broader, it is impossible to determine with accuracy whether the distribution of the disease has become narrowed or not during the centuries; and all contributions to this subject are but arbitrary combinations.

The significance of tuberculosis is evident from the enormous mortality with which it is yearly credited in the various countries. The larger the country, the more constant are the statistics through a term of years. For the year 1894, for example, the conditions were as shown in the table following.

The preëminence of tuberculosis among diseases may be estimated by a comparison of the number of its victims with those of the infectious diseases which are most dreaded and are notoriously most widely distributed.

In Germany, during 1894, there were the following mortality records:

Diphtheria and croup	63,701
Whooping-cough	21,521
Scarlet fever	8,937
Measles	16,173
Typhoid	6,373
Total	116,705
Tuberculosis	123,904

Tuberculosis alone, therefore, with its 123,904 deaths, exceeds the combined mortality of all the other infectious diseases above mentioned.

	Population, Dec. 2, 1895.	Mortality Exclusive of Tuberculosis.	Mortality through Tuberculosis in General.	From Pulmonary Tuberculosis Alone.
Prussia	31,849,795	679,793	74,656	71,133
Bavaria	5,797,414	145,826	18,175	16,610
Saxony	3,783,014	87,228	9,023	7,916
Würtemberg	2,080,898	50,606	5,047	4,322
Baden	1,725,470	39,583	5,059	4,940
Hesse	1,039,388	20,224	3,354	2,664
Brunswick	433,986	8,764	1,140	1,063
Saxe-Coburg-Gotha	216,624	4,051	480	418
Bremen	196,278	3,321	680	489
Hamburg	681,632	11,791	1,521	1,302
Alsace-Lorraine	1,641,220	37,436	4,769	4,177
German Empire	49,445,719	1,088,623	123,904	115,034
Further:				
Austria*	22,844,000	698,972		88,460
Italy†	30,000,000	791,606		54,279 3,510‡

In France, Sweden, Denmark, etc., it was unfortunately impossible to arrive at estimates comprising the entire population, since, as a rule, only the larger cities in these countries include the cause of death in the mortality reports.

Aside from the alarmingly high rate of mortality, tuberculosis gains an especial politico-economical significance from the fact that it gathers its victims not from children alone, whose maintenance and education represent but a slight outlay, but to an extent of more than 75 per cent. from the bread-winners, ranging between the ages of fifteen and seventy years. In this regard it is on an altogether different plane from diphtheria, pertussis, scarlet fever, and measles. Averaging the mortality reports for the years 1876 to 1891 in Prussia, the annual mortality from tuberculosis in the class of bread-winners, including the ages of fifteen to seventy, was 71,895, or a third of the entire number of deaths. Consumption runs a number of years before it proves fatal, but if we reckon the invalidism due to it at only one year, and the average loss of wage (or unemployed labor) at a value of two marks per day, then the loss of earnings for each person per year, 300 working days to the year, amounts to 600 marks; so for the total number of those who have died in the bread-winning period of life, 71,895 persons, the annual loss of earnings amounts to 43,137,000 marks annually. If we add to this figure the money for doctors and medicine, for food and care (counting that the sick pay out 2.19 marks per day), for burial, and, furthermore, the expenditures for invalids not included among bread-winners, we may estimate at least twice as much as the previous figure, or 86 million marks as the yearly cost of tuberculosis to the Prussian State. Consumption, therefore, demands an annual increase of the tax of 3.09 marks per head, or of 15 marks for each family of five, in the Prussian State.

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* Countries represented in the Reichsrath. Average of the years 1881 to 1890.

† Average of the years 1891 to 1893. The apparent rarity of tuberculosis in Italy is offset by a corresponding increased frequency of the fatal inflammatory diseases of the respiratory tract.

‡ Diseases of the larynx, of which a large percentage is constituted by laryngeal tuberculosis in Italy.

PART I.

ETIOLOGY OF TUBERCULOSIS.

CHAPTER I.

HISTORICAL SURVEY.

ANTIQUITY.

The history of tuberculosis* in the present sense of the word scarcely antedates the past century; nevertheless, at least one of the clinical manifestations of tuberculosis, namely, consumption, was known even in ancient times. There is a classical description of its symptoms as far back as Hippocrates (460 to 377 B. C.). He regarded it as a suppurative process of the lungs depending on so-called *φύματα*, by which term he understood, according to Virchow, circumscribed pus foci, and not, as the translation by the word "tuberculum" would indicate, actual tubercles in the modern sense. The same conception is held by Celsus (30 B. C.), Aretæus (*circa* 50 B. C.), and Galen (131 to 200 B. C.).

PERIOD OF ANATOMICAL RESEARCH.

Not until the middle of the seventeenth century, when the importance of anatomy first gained recognition and frequent autopsies were made, did the knowledge of tuberculosis make any notable advance. Nodules were discovered in the lung, which were described as tubercula or scirrhus; and genetic relationship between these and pulmonary phthisis was first maintained by Sylvius (1614 to 1672). He believed that they gave rise to vomicæ, considered them to be enlarged lymph-glands of the lungs, analogous to scrofulous growths, and credited both to an hereditary predisposition (*Dispositionem illam ad phthisin certis familiis hereditariam*). According to Morton

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* The following historical observations are based principally upon the thorough labors of Waldenburg and Predohl.

(1689), the tubercle was a necessary antecedent of the ulcerative pulmonary process. The theory of the glandular nature of the tubercle, as maintained by Sylvius, was then disputed by Morgagni (1682 to 1771), and was absolutely denied by Reid (1785) and Baillie (1794).

Magnetus (1700) was the first to describe miliary tubercles, but the discovery lapsed into oblivion, and these elements were to a certain extent re-discovered and their significance recognized by Stark (acc. to Reid—1785). Baillie then made a distinction between the nodules, which are aggregations of miliary tubercles, and the diffuse process, the so-called infiltrating tuberculosis or caseous pneumonia of later times. Common to both is the cheesy content, the scrofular, or, as Portal (1780) expressed it, the tuberculous matter. Suppuration of the nodules gives rise to consumption. A tubercle was for him a rounded tumor, with scrofulous content.

Hitherto the final result of the process, the pus and the cheesy matter, had been the focus of research. Bayle (1774 to 1816) was the first who based his researches upon the millet-like nodules, called by him tubercles, the development of which he followed from their solid condition to caseation and softening. From the simultaneous occurrence of these structures in all the various organs, he concluded that phthisis was not a disease peculiar to the lungs, and that it was not an outcome of inflammatory conditions, but that it was a constitutional disease, depending on the tuberculous diathesis (*dégénérescence tuberculeuse*), and that the formation of caseous material was the pathognomonic expression of this condition. *Phthisis tuberculosa*, a chronic specific disease of scrofular character, constitutes only a partial expression of phthisis as a whole, of which he distinguishes six types: (1) Phthisie tuberculeuse, (2) phthisie granuleuse, (3) phthisie avec mélanose, (4) phthisie ulcéreuse, (5) phthisie calculeuse, (6) phthisie cancéreuse.

In opposition to this complete classification, Laënnec (1781 to 1826) emphasized the regularity of the disease; he eliminated phthisie ulcéreuse (pulmonary gangrene) and phthisie cancéreuse (carcinoma of the lung) as separate diseases, and also phthisie calculeuse and avec mélanose as not belonging to phthisis in the proper sense of the word; phthisie granuleuse and tuberculeuse he then united into one group. Every phthisis, according to him, develops from tubercles. Phthisis and tuberculosis are therefore identical, and the tubercle is a fortuitous product of the lung, a neoplasm. With Baillie, Laënnec also distinguished between isolated tubercles, *i. e.*, circumscribed nodules, derived from aggregations of miliary tubercles, on the one hand, and tuberculous infiltrations, in which the tubercular material was not sharply definable but was diffusely spread over the lung, on the other. Tubercular infiltrations he believed to go through the same developmental stages as the isolated tubercle. At first it appears as a gray, tuberculous infiltration, at times gelatinous in character, then changes to a yellow infiltration, and finally softens, in the same manner as the isolated primary yellow tubercle. By the expression "tuberculous matter," which Laënnec likewise adopts, he denotes not the cheese alone, as do Baillie and Portal, but a substance which goes through the entire complex evolutionary process. The scrofules are in his eyes none other than a localization of tuberculosis in the glands.

Bayle and Laënnec exclude inflammation as a cause of phthisis. Broussais (1772 to 1838), on the other hand, in harmony with his irritation hypothesis, traces every phthisis to an inflammation, and regards it as a chronic pneumonia with a tendency to destruction of the lung. The tubercles are accordingly not neoplasms but the product of the inflammation.

About this time Gendrin first recorded the presence of a millet-like granulation in the lung of the calf.

Laënnec's theory found a warm advocate in Louis, an opponent in Andral. The latter regarded the tubercle not as a neomorph but as an originally fluid secretion, which, like pus, became inspissated and caseous as a result of a special tubercular predisposition of the organism, and under the influence of inflammation or congestion.

The translation of Laënnec's work by Meissner (1832), as also Canstatt's influence, gained a following for this teaching in Germany. According to Rokitansky (1842), the tubercle is an exudate composed of inspissated proteins; tubercles and scrofulous glands are identical structures. As one of the followers of the then recently developed doctrine of dyscrasias, he considered a predisposition on the part of the organism, the tuberculous habitus, as of very especial importance.

We may record, as scientific curiosities of the time, that von Eichmann, Furnivall, and Seydlitz associated tubercles with changes in the central nervous system and the sympathetic nerves, while according to Dupuy and Baron tubercles were a species of hydatid formation.

Meanwhile the doctrine of dyscrasias gave occasion to numerous chemical researches (von Preuss, Simon, Lehmann, Vogel), the object of which was to elucidate the anomalous conditions of the blood and the exudates. Yet these researches threw no further light upon the problem of tuberculosis.

Far more fruitful were the microscopic investigations which under Gluge's stimulus (1841) became more popular. In 1844 Lebert found certain irregular, angular, non-nucleated cells in the isolated tubercles and in tuberculous infiltrations, and these he considered pathognomonic, calling them tubercle corpuscles. This was vigorously contested by Henle and Reinhardt (1847), the latter of whom demonstrated that the tubercle corpuscles could arise in pus, and that, consequently, they could have no specific importance.

We cannot expect in this place to describe even summarily the many hypotheses to which almost every clinician and every pathologist has contributed his own. Virchow attempted to establish order in the midst of these contradictions and misunderstandings by formulating the doctrine (1847) that caseation was not a process peculiar to tuberculosis, but was only one of the various forms of retrogressive metamorphosis. In 1852 he limited the term "tubercle" to miliary tubercles, occurring as organized, non-vascular, cellular neoplasms. The tubercle, according to him, may become caseous, or calcified, or undergo fatty degeneration, and in the latter case become absorbed; that is to say, healed. Virchow separated caseous pneumonia from typical tubercle formation or tuberculous phthisis, and founded the duality theory, which early found a clinical exponent in Niemeyer (1866).

In 1857 came Buhl's discovery that acute miliary tuberculosis was, as a rule, traceable to preëxisting cheesy foci, whose infectious products were taken up by the blood and so gave origin to disseminate miliary foci in the various organs. He thus had the conception of miliary tuberculosis as a specific disease due to absorption and infection.

Under the influence of Laënnec's teaching, especially in France, scrofula came to be regarded less and less as an independent disease. The absolute identity of the scrofular and tubercular diathesis was defended by Rilliet, Barthez, and Cruveilhier (1862). The problem of tuberculosis had reached a stage at which it could not hope to gain anything further from purely anatomical observations.

PERIOD OF EXPERIMENTAL INVESTIGATION.

We now enter upon the period of experiment. Even Morgagni had definitely expressed his conviction that phthisis was infectious, and this belief has never since failed of a following among physicians, especially in certain countries. Laënnec and Albers describe certain nodules, which from the description seem to have been anatomical tubercles, resulting from wounds received at the autopsies of tuberculous bodies. Laënnec says, according to Demme, that he cut himself at such an autopsy, and thereafter began to feel sick and showed the first signs of phthisis. Nevertheless, the early attempts to produce the disease by artificial infection were failures. Kortum (1789), Hebreart (1802), Salmade (1805), Lepelletier (1816), and others, had inoculated themselves, healthy children, and animals with scrofulous pus, but with no effect. Moreover since tubercle-like nodules are produced in the lung by the injection of quicksilver into the trachea and the bronchi (Cruveilhier), the theory of infection at first found no foothold. Klencke (1843) was the first to announce that he had injected tubercle-cells taken from miliary tubercles and from tubercles in the stage of gray infiltration into the jugular vein of rabbits, and that at the autopsy twenty-six weeks later he had found a widespread tuberculosis of the liver and lungs. It is undetermined whether Klencke himself appreciated the significance of his discovery; at any rate, his contribution was forgotten and remained without influence upon the theory of tuberculosis.

The ingenious and broadly conceived experiments of Villemin had to a certain extent a brilliant result and raised a storm in the medical world at the time of their publication (December, 1865). He inoculated rabbits with matter taken from the gray and yellow tubercles of phthisical individuals, by subcutaneous injections into the tissue behind the ear, and found that they regularly developed tubercles in the lungs; whereas uninoculated rabbits, or those inoculated with pus, showed no trace of tuberculosis. This brought him to the conclusion that phthisis was a specific disease, virulent in type, and produced by an inoculable agent. He attained the same results later on by the injection of caseous material, of phthisical sputum, and of infectious material from a tuberculous cow. In spite of repeated corroboration, the researches of Villemin did not achieve universal recognition, for they were heavily counterbalanced by the authority of certain writers (Aufrecht, 1869, Talma, 1881, and others) who maintained that they had also produced tuberculosis in animals by the inoculation of non-tuberculous material, such as pus, particles of sponge, and so on. The confirmation of these researches would necessarily deprive the doctrine of specificity of all support. Further trials, however, by Ponfick (1869), Chauveau, Klebs (1873), Baumgarten (1880), and

Cohnheim, demonstrated that these results were entirely attributable to faulty experimentation and accidental infection of the animals. Further, the feeding and inhalation experiments described below, as also the inoculations into the anterior chamber of the eye, contributed materially to undermine the objections of the opponents of the doctrine of specificity.

Hand in hand with these experimental labors, and in part owing to them, went numerous histological investigations into the structure of the tubercle and its constituents (Wagner, 1870, Schüppel, 1871, Virchow, etc.). Even before this time, Rokitansky had found polynuclear cells in the tubercles, and Virchow had frequently described them. The significance of these giant cells was recognized and established by Langhans. A prolonged discussion now dragged along as to the origin of these giant cells and their pathognostic importance, which was defended by one party and was disputed by others, notably Virchow, Klebs, Heryng (1873), Ziegler (1875), Orth and Baumgarten. The latter won the day, inasmuch as they demonstrated the giant cells in non-tubercular inflammatory tissue, as surrounding foreign bodies and parasites. Lichtheim also found them in atelectatic areas after ligation of a bronchus.

The domain of tuberculous disease was enlarged by the discovery of tubercles in fungous joint-affections (Köster, 1876), in hyperplastic lymph-nodes (Schüppel), in lupus (Friedländer, 1873), and in cold abscesses (Lannelongue); and Friedländer was led by his researches to the conception of a local tuberculosis, which he systematically developed.

In the mean time the duality doctrine of Virchow was accepted with certain modifications by Waldenburg, Aufrecht, and Rühle; while, on the other hand, the unity theory of Laënnec gained fresh support from the results of experimental investigations. The latter was defended, and further substantiated by the researches of Rindfleisch, Baumgarten, and Cohnheim, and culminated finally in the doctrine that tuberculosis included all affections the inoculation of which upon suitable animals resulted in that disease. The same theory was embraced by Grancher, Lépine, Charcot, Brissaud, and Cornil in France, by Wilson and Fox in England, and by Sangalli in Italy.

Since the infectiousness of tuberculosis had thus been almost demonstrated by experiment, the question of the virus, of its nature and quality, became ever more prominent. The assumption that the *materies morbi* was developed under the action of some irritant in the body itself, possibly out of the disorganization products of the cells, must have seemed improbable to any one acquainted with the recent advances in science, especially with the epoch-making work of Pasteur. Everything seemed to indicate that there was a *contagium vivum* which forced its way into the body and there proliferated. Most probably the agents of the disease were bacteria. Klebs (1877) thought that he had discovered the virus in the Monas tuberculosum, an organism which he isolated by fractional cultivation and of which he proved the virulence by inoculation. His conclusions were accepted by Schüller and Reinstadler. Toussaint (1881) also grew bacteria from tuberculous blood, the inoculation of which produced tuberculosis a number of times. At the present time I need hardly do more than to say that both authors, with their bacteria and cocci, missed the real agents in tuberculosis.

KOCH'S DISCOVERY.

It was reserved for Robert Koch to bring the problem of the nature of tuberculosis to a final solution. After many unsuccessful attempts, he was finally able to demonstrate fine, rod-like structures, subsequently called tubercle bacilli, in sections of the fresh, gray, pulmonary tubercles of recently killed animals. This was done by the use of the methylene-blue solution to which potash had been added, and by differential staining according to Weigert's method, and was facilitated by the marked improvements in optical apparatus introduced by Abbé.

These bacilli were found by Koch regularly in miliary tubercles, in tuberculous intestinal abscesses, in scrofulous cervical glands, in fungous bone and joint disease, in lupus, in phthisical sputum, in the consumption of cattle—in brief, in all diseases which by their course as well as by their microscopic structure, and the infectious nature of their products, must be regarded as tuberculous. The constancy of their presence pointed to a certain connection between the bacilli and the pathological processes, and a genetic relationship was rendered even more probable by the fact that in further investigations the bacilli were found exclusively in tuberculous, never in other diseases, nor in healthy tissues, and that they could be demonstrated even in the very inception of the disease.

In order to prove that the bacilli were not a disorganization product of the tissue (metaplastic cellular bioplasm of Wiegand), but actual organisms, with the signs of independent existence, it was necessary to cultivate them outside of the body on artificial media. At first they refused to grow upon the customary media; but Koch finally succeeded in developing them at a temperature corresponding to that of the blood, and upon coagulated blood-serum previously sterilized by Tyndall's method.

The keystone of Koch's demonstration was his inoculation test, whereby he showed that pure cultures obtained by a series of transplantations and freed from all the accessory products of the disease, if injected with precautions to exclude all the sources of error in previous researches, would still produce tuberculosis as typical as that due to the inoculation of infected tissues with miliary tubercles, cheesy glands, cattle tubercles, lupus, etc. These results were based upon experimentation with 172 guinea-pigs, thirty-two rabbits, five cats, etc. Simultaneous injections of the most various substances, containing no tubercle bacilli, were always negative in hundreds of guinea-pigs and rabbits.

This classical demonstration, which Koch published in 1882, was fortified and absolutely corroborated by the numerous control experiments which were everywhere instituted. Isolated contradictory reports from Spina and others found an explanation in the faulty technic of the authors. Schmidt held that the tubercle bacilli were fatty acid crystals, Gregg that they were fibrin filaments.

The question of the etiology of tuberculosis thus finally settled, tuberculosis was classified among the infectious diseases, and the tubercle bacillus was recognized as the sole cause of the disease. The enormous value of this step for diagnosis need not be further presented. The etiological identity of miliary tuberculosis with caseous pneumonia, scrofula, the fungoid processes lupus, and cattle tuberculosis was at once firmly established.

CHAPTER II.

THE TUBERCLE BACILLUS.

A short time after Koch had published his first observations, Baumgarten affirmed that independently of Koch he had been able to find bacilli identical with those of Koch, by clearing up tuberculous tissue with very dilute potassium or sodium hydrate. He attempted to demonstrate the specific significance of this bacillus in tuberculosis by histological methods.

STAINING METHODS.

In the living condition, and examined according to Koch's procedure in the hanging drop, the tubercle bacillus is identified as a small, non-motile rod. In order to develop the finer details, especially the relations to its surroundings, it is necessary to stain the organism. The original method of Koch, as above described (page 26), was considerably improved by Ehrlich, and, with certain modifications suggested by Weigert and Rindfleisch, still finds wide application.

To prepare **Ehrlich's stain,** 5 cc. of pure anilin oil are mixed with 100 cc. of distilled water, the mixture well shaken, and then passed through a moist filter. To the clear watery filtrate, a saturated alcoholic solution of methyl violet, or better fuchsin (20 gm. of the stain to 100 or 150 cc. of alcohol), is added drop by drop, until there is a faint opalescence—according to Weigert, 11 cc. of the stain to 100 cc. of the anilin water.

The disadvantage connected with Ehrlich's method is that the stain must always be freshly prepared, on account of the instability of the anilin water. This is only very temporarily remedied by the addition of 10 cc. of absolute alcohol.

The **Ziehl carbol-fuchsin solution** marked a very distinct advance, since it kept for practically an indefinite length of time, and so became universally adopted. It is prepared by rubbing up 1 gm. of fuchsin in 10 cc. of absolute alcohol, and then adding this mixture to 100 cc. of a 5 per cent. solution of carbolic acid in water. The method was further simplified by Rindfleisch, who reduced the time of staining (from twelve to twenty-four hours), by the use of heat, to a few minutes.

Various authors suggested a multitude of more or less important modifications of the stain, but I shall have to content myself with a mere reference to the comprehensive survey of these contributions in the writings of Unna, Czaplewski, Heim, and others. The important thing still is that one should continually practice and gain control of one or two of the approved methods. As a simple and reliable method for determining the presence of tubercle bacilli the following mode of procedure has been widely employed:

A small particle of the material selected in case of sputum from various places, especially those which appear suspicious, is spread over a clear cover-glass in a very thin smear, by means of a strong platinum loop, previously sterilized by heating. The glass is seized with a Cornet's forceps, carefully dried over a flame, and the preparation is "fixed" by drawing the glass three times slowly over the flame. A strongly concentrated Ziehl's solution is then dropped on the smear so as to cover it completely, and this is brought to the steaming point (not to boiling!) by carefully moving it over the flame (one-half to one minute). The stain is then washed off with water, and the cover-glass agitated for a short time in a 2.5 per cent. solution of sulphuric acid, until the color has disappeared, and only a reddish tinge remains. The cover-glass is then plunged into absolute alcohol, washed with water, and stained with a dilute watery solution of methylene-blue (or malachite green) for one-fourth to one minute. After further washing with water, the preparation is carefully dried by heat or absorbent paper, and is finally mounted in a drop of immersion-oil, or, if a permanent preparation is desired, in Canada balsam. It may now be examined upon the slide. (See further on rapid staining, in the chapter on Diagnosis.)

In case of sections which do not stand intense heat, the mode of procedure is somewhat altered. The sections are placed in a dish containing the Ziehl solution, which is then kept for from one to twelve hours in an incubator at a temperature of 37° C. The sections are then put into water, transferred for a moment to 2.5 per cent. sulphuric acid, thence into 60 per cent. alcohol which has been diluted with either nitric or sulphuric acid in the proportion of 20 drops to 100 cc. After the alcohol bath the sections are thoroughly washed in water, differentially stained with methylene-blue, again put into alcohol, and finally mounted. In this manner very beautiful preparations are made, in which the tubercle bacilli are stained red, while the surrounding tissue, the cells, nuclei, and the other bacteria, which are especially abundant in sputum, are stained blue.

MORPHOLOGY OF THE TUBERCLE BACILLUS.

Examined in the stained preparations, with an oil-immersion, Abbé's illuminator, and an open iris diaphragm, the tubercle bacilli appear in the shape of slender rods, varying in size, but on the average equaling one-fourth to one-half the diameter of the red blood-cell—*i. e.*, 0.0015 to 0.004 mm.—in length. They are either regular in contour, or represent a slight notching or flexion, and in young cultures are generally shorter than in old or than in sputum. In the latter one occasionally finds fairly long, thread-like or chain-like colonies of bacilli. They lie isolated, or sometimes in small groups and bundles; more rarely and only in careful preparations, in the form of strands.

VACUOLE-SPORE FORMATION AND INVOLUTION.

Oftentimes the bacilli are not homogeneously stained, but at regular intervals present a number of unstained, clear areas, with delicate stained contours. As the unstained bacilli also show highly refractive corpuscles of similar appearance, Koch held the two to be identical, and concluded that the condition was not one of vacuolation, of simple breaks in the protoplasm, but of true spore-formation. Flügge has described these clear areas as of ampullar type, protruding laterally beyond the true margin of the bacillus. At that time there was a general tendency to regard them as the expression of a retrogressive metamorphosis, in fact, as vacuoles.

It is frequent enough, particularly in old cavities, to find the bacilli broken up into a line of short fragments, an appearance which is undoubtedly due to degeneration.

Von Metschnikoff, Nocard and Roux, and also Czaplewski, were struck by the fact that after very deep staining with carbol-fuchsin or anilin-fuchsin and subsequent decolorization, isolated bacilli show small, round corpuscles, in color dark to black, which give it a granular appearance. With prolonged decolorization, the substance of the bacilli loses the stain, while these round or ovoid bodies retain it, so that chains of small, round, red-stained granules—the granular bacilli of Biedert and Siegel—are developed. Babes and Czaplewski succeeded in bringing these spores out by double staining in exactly the same manner as true spores. The spore character of these structures is attested also, in addition to the regularity of their contour, by their resistance to staining and the tenacity with which they retain the stain, when once taken up, in the face of acid (Neisser's spore-reaction); but there are no reliable data regarding sporulation. They have, indeed, a somewhat increased, but by no means the characteristically high resistance to heat, desiccation, and antiseptics which we are accustomed to regard as the specific attribute of spores.

If, therefore, we still maintain the sporular character of these structures, we must assume at least that they are endowed with a very minor degree of vitality.

PLEOMORPHISM AND CLASSIFICATION.

In old cultures one finds at times swollen, elongated forms with lateral buds (Roux and Nocard), branches with club-shaped swellings, which von Metschnikoff designated involution forms. Further pleomorphic forms were described by Maffucci as thread-like structures branching like a mycelium. Klein described dichotomous and lateral branches attached at a right angle. Fischel and Koppen Jones compared these various forms with the growth phenomena of actinomyces, and assume a family relationship between the two groups.* All these questions, however, still await a final settlement.

Specific Staining Reaction.—These various forms have no immediate importance in practice, since we have to deal, for the most part, only with longer or shorter rodlets, continuously or interruptedly stained. Our staining methods are not only adapted to demonstrate the bacilli distinctly, but their chief value lies in their diagnostic import. With these methods, the tubercle bacilli have the unique and almost specific power of retaining the primary stain, whereas the tissues and all the other bacteria surrender the stain to the decolorizing fluid and later take up the secondary color. The cause of this resistance to acids is considered by Unna and others to lie in the fatty content of the bacilli. The diagnostic value† of these specific reactions is not impaired by the fact that they are shared to a certain extent by other structures: namely, horny tissues, hair, the epidermis, the large oval spores of a certain large species of bacteria found by Koch in the gut, the spores of moulds, and also a certain species of yeast. The very manifest morphological differences between these other structures and the tubercle bacilli render it almost impossible even for the tyro to confuse them. Similarly there is no difficulty in distinguishing from the bacteria certain rod-like crystals of the fatty acids (pseudobacilli of Celli and Guarnieri), which according to these authorities may present similar staining reactions.

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* Friedrich asserts that in animals also he has found radiating fungus-like modes of proliferation.

† Ferrán held the tubercle bacilli to be identical with the B. spermigenes described by him. This has been disputed by Zupnik on good grounds, and attributed to imperfect bacteriological methods. A. Moëller described two species of bacilli, the timothy and the dung-bacillus, which are grown from plants, and which resemble tubercle bacilli in their resistance to acid and alcohol, and in their rapid growth.

DIFFERENTIATION BETWEEN THE BACILLUS OF TUBERCULOSIS AND OF LEPROSY.

Koch himself found that the only bacilli which stained like the tubercle bacilli with the ordinary methods were Hansen and Neisser's lepra bacilli, and these are so similar in form and size that confusion is almost inevitable. Although this danger naturally hardly presents itself in non-leprous communities, yet it might give occasion to frequent diagnostic errors in places where leprosy is more common, especially as the clinical phenomena are in certain cases somewhat analogous. Least valuable in the differentiation between these two forms are the morphological peculiarities. The tapering of the lepra bacillus at one extremity, described by Neisser, could not be made out with certainty by Baumgarten. This is far too subtle a distinction to be of working value. A better criterion is the arrangement and the situation of the two species in the tissues (Babes), the lepra bacilli having by preference an intracellular position, the tubercle bacilli, as a rule, an extracellular. The former are distinguished by the density of their grouping within the cell; they are often found as almost solid, rounded masses of bacilli, which entirely obscure the nucleus. The tubercle bacilli lie simply within the cellular protoplasm, and arrange themselves in small, star-shaped clusters, within and between which a large part of the cell-body is always to be seen. There are, however, many variations from this schema.

Unna, as the outcome of a desiccation method elaborated by him, opposed the belief in an intracellular location with the assertion that the groups of bacilli in question did not occupy the cells, but lay free in the lymph-channels; and that the misconception came from confusing the mucous covering of these masses with cellular protoplasm. As is well known, a fierce dispute raged over this subject. After a long period of rest, it was again taken up by Bergengrün, and finally settled according to Unna's interpretation.

Relatively the best results are furnished by differential staining.

There is a quantitative difference between the two species in the appropriation of the stain, inasmuch as the lepra bacilli take up the color considerably faster than do the tubercle bacilli. The former also have the power of staining in dilute, cold, watery solutions, which is not shared by the tubercle bacilli, and this point has been made the basis of a method of differentiation by Baumgarten.

1. For cover slip preparations: The cover-glass is allowed to float for six or seven minutes upon a dilute alcoholic solution of fuchsin (five or six drops of the saturated alcoholic solution to a watch-glass of distilled water), the preparation is then decolorized for one-fourth of a minute in a mixture of one part sulphuric acid to ten parts of alcohol, is well washed in distilled water, just covered with a watery solution of methylene-blue, and must be examined in this fluid without delay by means of the oil-immersion. The lepra bacilli are distinctly stained red, while the tubercle bacilli are unstained.

2. For sections: They are brought for ten or fifteen minutes into a dilute, alcoholic solution of fuchsin, decolorized for one-half minute, washed off, then dehydrated for three or four minutes in absolute alcohol, and examined in oil of bergamot.

These methods have been found to give good results in a large number of tests; yet in isolated cases failures have also been recorded (Wesener).

DIFFERENTIATION BETWEEN THE TUBERCLE AND THE SMEGMA BACILLUS.

The smegma bacillus has the same staining reactions as the tubercle bacillus. Confusion is especially apt to arise when the material comes from regions which are known by experience to be the favorite haunts of the smegma. These infest by preference the corona glandis, the scrotum, the skin between the thigh and the scrotum, and, further, the external genitalia of women of all ages, especially the interlabial fold. In general, the collection of the cutaneous secretions seems to be the condition favoring their development. Gottstein and Bitter found them in cerumen, and Laabs detected them in the most diverse situations over the body-surface, at all the natural openings to the exterior, even within the coating upon the tongue and teeth.

The practical importance of an accurate differentiation between the two is best demonstrated by the fact that confusion between them has been known to occur, and has even occasioned operative interference. Laabs records a case which came to operation on account of the supposed presence of tubercle bacilli in the urine, but in which, instead of the disease of the kidneys which had been inferred, there was an abscess of the lumbar region. A kidney which had been extirpated on account of a similar finding in the urine was studied by Mendelsohn, and presented the pathological picture of a stone in the pelvis of the kidney. König and, later, Bunge and Trantenroth, recorded similar cases. It is, therefore, justifiable to enter more into detail upon the subject of differentiation. A granular appearance of the bacilli, a moniliform disorganization (*vide* Leyden), especially a grouping into strands or rows, as is found at times in genito-urinary tuberculosis, speaks for tubercle bacilli; but no more reliable indication than this is to be gained from the morphological features.

Here, also, modifications of the staining technic stand us in good stead. All methods which employ inorganic acids as decolorizers have been found to be absolutely useless for differential purposes. Further, the organic acid suggested by Alvarez and Tavel and Klemperer, namely, glacial acetic, does not give a constant result with the varying conditions of the smegma bacillus (Markus). Far more valuable is the method of Weichselbaum, tested by Grethe.

The preparation is stained in the usual manner with carbol-fuchsin, washed, and then, without further decolorization, is treated with a concentrated solution of methylene-blue in absolute alcohol;* the tubercle bacilli remain red, while the smegma bacilli take up the blue stain. Honsell employed the following method for the more resistant forms of the smegma bacillus: carbol-fuchsin, water, drying, decolorization in acid alcohol (absolute alcohol 97.0, HCl 3.0) for ten minutes, washing, differential staining in a mixture of water and alcoholic methylene-blue in equal parts.

Somewhat more complicated and equally reliable is the procedure of Czaplewski. After treating with heated carbol-fuchsin, the superfluous fluid is allowed to drain off, the preparation is bathed for about five minutes in fluorescein-methylene-blue, then from one-half to one minute in a concentrated alcoholic solution of methylene-blue, after which the cover-glass is rapidly washed in clean water, and is examined in the usual manner.†

In using this method, Bunge and Trantenroth found that after five minutes' decolorization in the great majority of the preparations all the smegma bacilli were decolorized, and only rarely did they find one or more bacilli, reddish-violet in color, but by no means so intensely stained as before. Tubercle bacilli seem to stand the decolorization for as much as fifteen minutes without ill effect. These methods, although efficient as a rule, may yet fail in exceptional cases. The above-named authors have therefore elaborated a procedure which, according to their reports, has never yet failed them. It is described as follows:

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* Bunge and Trantenroth emphasize the importance of using absolute alcohol.

† A concentrated solution of yellow fluorescein in alcohol is decanted, methylene-blue added in excess, and this solution again decanted off.

Fixation (and removal of fats) of the smears by absolute alcohol for three hours; then 5 per cent. chromic acid for at least fifteen minutes, and careful washing in several changes of water. Staining with carbol-fuchsin, decolorization with sulphuric acid (diluted) three minutes, or nitric acid (pure) one to two minutes, secondary decolorization combined with secondary staining in a concentrated alcoholic solution of methylene-blue for at least five minutes. In none of the many smegma preparations taken from various individuals could smegma bacilli be detected when treated by this method, although in the control preparations they were always numerous. Tubercle bacilli were distinctly stained red, even when the preparations were kept in absolute alcohol as long as twenty-four hours, in the chromic acid up to one hour, in the dilute sulphuric acid seven minutes, and in the alcoholic methylene-blue as much as twenty minutes.

The authors somewhat qualify the reliability and utility of their method by the admission that in their control experiments with tubercle bacilli they employed only sputum, and not tuberculous urine, which in practice, of course, always gives the occasion for a differential diagnosis of this sort. Moreover, as the authors themselves admit, it is just in pathological urine with prolonged ammoniacal decomposition that both smegma and tubercle bacilli evince a greater sensitiveness to decolorization media than they do in the sputum, even to such an extent that they do not resist decolorization according to the methods of Weichselbaum and Czaplewski. For such cases, Bunge and Trantenroth advise that the smegma bacilli be kept separate by mechanical means. They base this upon the fact that the orificium extern. urethræ shelters tubercle bacilli but rarely; and that they found, at least in the seven cases tested, that urine passed in the natural way, even after thorough cleansing of the orifice, contained smegma bacilli, whereas that collected through the catheter was free.

In important cases, therefore,—as, for example, when an operative procedure depends entirely upon the finding of bacilli in the urine,—one could hardly feel satisfied, after all that has been said, with a diagnosis based exclusively upon the staining reactions. Laser and Czaplewski have lately succeeded in growing pure cultures of the smegma bacillus upon agar mixed with human blood, *i. e.*, nutrose-serum agar. As the smegma bacilli show an undeniable growth even after twenty-four hours, whereas the tubercle bacilli need at least a week, cultivation may afford a valuable differential point.

In case, however, certainty cannot be attained in any other way, one would be obliged to have recourse to animal experimentation, which when properly employed yields absolutely positive results, especially with reference to tuberculosis, and which in my opinion is far less difficult and complicated than is usually supposed. (See chapter on Diagnosis.)

[The term pseudo tubercle bacilli is now generally applied to those micro-organisms which resemble the bacillus of tuberculosis only in form and in their failure to be decolorized by acids. They differ from it in their relation to temperature, being less sensitive to this factor, in the fact that their growth is much more rapid, and especially in their feeble pathogenicity. Researches of the past three years have proved that they are more widely diffused than had been supposed. They occur for the most part outside the body, and though many of them are experimentally pathogenic, but few have been found to be the causative agents of disease. Moeller found them in feces, Benenuti in gangrene of the lung. Hoelscher inoculated into animals the acid-resisting butter bacillus of Rabinowitsch and Moeller, and found that in pure culture it had some virulence, but did not produce a condition identical with tuberculosis. Kayserling found them in hay, especially timothy, and in seeds; also in cultivated earth, and in the products of herbivorous animals, as milk and butter. Moeller found them in human sputum, where they may easily cause errors in diagnosis. He advises the following method of differentiation: Mix the suspicious secretions with sterile bouillon, keep it at 30° C., and if a rapid growth occurs, —that is, in two or three days, it is the pseudo tubercle bacillus. Lichtenstein has found this organism several times in human sputum in cases of gangrene of the lung and in catarrhal bronchitis. He believes that it occasionally causes an incorrect diagnosis of phthisis. R. Koch compared the two bacilli with reference to their agglutinations. He took the serum of animals treated by attenuated cultures of tubercle bacillus for purposes of immunity, and found that it agglutinated not only the tubercle bacillus, but the pseudo tubercle bacillus, that is, the bacillus of bird and of fish tuberculosis, the Arloing Courmont bacillus, the butter bacillus, and the hay bacillus of Moeller. The reverse of this he also found to hold good; that is, serum from animals immunized from the pseudo bacillus agglutinated the true tubercle bacilli. Herr finds the pseudo bacilli very widely distributed in earth, cow dung, hay, etc., and concludes that they originate in the earth.

In general, it may be said that the pseudo tubercle bacilli are coming to occupy a more and more prominent position in bacteriology, that they may cause errors in diagnosis, and that their recognition is not at all easy. There are cases in which a positive conclusion can be arrived at only after inoculation of the suspected matter into animals. There is an interesting similiarity betwen the pseudo tubercle bacillus and those cultures of the true tubercle bacillus that have been attenuated by propagation on artificial media for many years through many generations, a similiarity in their morphology and in their feeble pathogenicity, and this similiarity is emphasized by the results of Koch's experiments upon their agglutinating properties as above quoted.

Birt and Leishman have recently added another to the list of acid-resisting bacilli, having isolated it from a case of chronic bronchopneumonia. The list now numbers nearly thirty. Abbott and Gildersleeve, and Klemperer, conclude that a close relationship exists between these and the tubercle bacillus The latter believes that their differences in virulence and in morphology are not fundamental, but have resulted through adaptation to various environments; he believes that the tubercle bacillus may be considered an acid-proof saprophyte that has subsequently become a parasite.—Ed.]

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BIOLOGY OF THE TUBERCLE BACILLUS.

CULTIVATION.

Although the specific staining reaction suffices to identify the tubercle bacillus in the majority of cases and for most practical purposes, nevertheless artificial cultivation outside of the body is essential for many problems of finer diagnosis, and especially for the study of biological relations. Koch had already shown that the bacilli are not adapted to grow upon the ordinary media, gelatin, etc., at the temperature natural to them. He succeeded in producing a growth only upon blood-serum.

Young fresh tubercles taken from recently killed animals furnish a favorable source for pure cultures. Koch, however, succeeded in procuring cultures also from closed cavities, from lupus, etc. If the body is old, and if, as always occurs in cavities and at times even in miliary tubercles (see Mixed Infection), there has been a considerable secondary invasion of the selected focus by other forms of bacteria, the cultural experiment is so much the more likely to miscarry, since the secondary forms early take possession of the entire medium as a consequence of their more active growth. It is not possible to isolate the true agents in the disease by means of the usual "plating" methods which succeed so well, for example, in case of the anthrax bacillus, since the tubercle bacilli fail to show any notable growth upon the plates, possibly in consequence of deficient aeration.

Under certain circumstances it is possible to secure cultures even from sputum, by means of a method suggested by Koch.

The sputum—naturally only that which comes from the lungs—is washed several times with running water, and so freed from the bacteria contributed by the upper air-passages. A small particle is then torn from the center of the mass, and microscopically examined. If one is convinced that only tubercle bacilli are present, and that it is not simply a case of secondary infection, a second particle is withdrawn, again from the center, and is brought over to the nutrient medium with good prospect of success. Colonies produced in this way differ, according to Kitasato, from those grown from the tissues, in having a moist, glistening, smooth appearance.

Serum Cultures.—In planting the tuberculous material, one rubs it thoroughly into the medium by means of a platinum loop. If the particles are of more solid consistency, the contained bacteria are liberated by crushing the tissue between two sterile scalpels or slides, and a more uniform distribution over the surface of the medium is thus secured. All procedures demand the most careful asepsis, since otherwise contamination occurs, as is revealed in a short time by turbidity of the excess water or by the rapidly spreading colonies.

Growth of the Serum Cultures.—If the media, properly prepared with blood-serum, are kept in the incubator at a temperature of 37° C., no change is at first to be made out. Only after the fifth day, as has been described by Koch, can we discover fine, dull white points upon the surface with the use of the loop, and these gradually increase to small, dull, dry scales. The scales continue to increase in size, become confluent, and give rise to a thin, dull, grayish-white covering. This is more loosely attached the firmer the medium is, and may often be lifted off in large films.

The colonies do not liquefy the serum and do not penetrate into it, but keep to the surface, forming a thin, dull pellicle, which often grows to the height of several millimeters along the opposite side of the test-tube.

Younger colonies appear under a magnification of 80, as delicate S-shaped growths, their course wavy and their extremities tapering. By means of a Klatschprëparat, the configuration may also be studied in a stained condition. The single bacilli do not lie directly next to each other,—that is, they do not seem to touch,—but are separated by a clear though minute interval. This interval was interpreted by Koch as a cement-substance, which insures the unity of the colony.

Glycerin Media.—The serum cultures demanded so great an amount of time, industry, and technical elaboration, that few investigators have given their labors to this field. We must therefore consider that a notable advance was achieved in the study of tuberculosis by the discovery of Nocard and Roux that the addition of glycerin, as a hygroscopic agent, converted the bouillon and bouillon agar, which were easily made but were unsatisfactory for growing the tubercle-bacilli, into splendid media.

Episode of Misunderstanding.—A memorable episode of misunderstanding in the history of tuberculosis dates from this time, inasmuch as various communications from the most prominent French investigators met with unanimous opposition in Germany. Even the descriptions given by Nocard and Roux of the glycerin-agar cultures did not agree with the conditions found in Germany. Further, the pathogenic characteristics seemed, according to the French investigators, especially Yersin, to have been suddenly altered by cultivation upon glycerin-agar, a fact which was not corroborated in Germany. Metschnikoff grew bacilli at 43.6° C., whereas Koch found that all growth was inhibited at a temperature over 42° C. Experimental cures were achieved with various remedies in France, whereas I invariably lost my animals, in spite of all remedies, within the same time.

At first, on account of the imperfect communication between Berlin and Paris, these extraordinary discrepancies found no explanation. When the first Parisian tuberculosis cultures came to Berlin, and when, shortly afterward, similar cultures were in most friendly fashion put at the disposal of the author in the Pasteur Institute in Paris, their unusual appearance could not but be admitted. The riddle was, however, soon to be solved.

Chicken Tuberculosis.—Ribbert, and especially Rivolta, had discovered differences between chicken and human tuberculosis, Maffucci had determined these differences more precisely, and Koch finally proved the identity of cultures made from chicken tuberculosis with those which were sent from Paris. It was now established as a fact that Nocard and Roux had made use of the tuberculosis of a pheasant as the source of their cultures, whereas the German cultures were traced to human tuberculosis.

A realization of these facts is necessary in judging of the work done during this era of misunderstanding, especially in France. For not only did Nocard and Roux employ cultures of avian tuberculosis, but also many other investigators, who borrowed their cultures from this source instead of making original inoculations. Thus it was that the confusion for some time was widely spread. The further studies of Maffucci, Straus and Gamaleia, in addition to those already mentioned of Koch, rendered still more exact the differential diagnosis between avian and mammalian tuberculosis, as will be detailed later in so far as is necessary for our purposes. Whenever we speak simply of tubercle bacilli, the disease germ of human tuberculosis is always understood.

Growth of the glycerin-agar culture colonies, grown upon 4 to 6 per cent. glycerin-agar in distinction to the serum cultures already described, form within a few days crumbly, irregular, whitish-yellow, dull or slightly refractive pellicles. In their further development they give rise to well-marked, raised granules or warts, occasionally with sinuous outlines, and often with a scaly areola. With a rich sowing, they form very profuse, thick vegetations, which assume a more yellowish to brownish-yellow or even reddish tinge with age, and emit a characteristic aromatic odor.

In order to produce a luxuriant culture from weakly developed colonies, especially from such as are grown directly from the tissues, it is well to transplant the first two or three generations very early, about every eight to fourteen days, to new media.

Fluid Media.—The development of tubercle bacilli is extremely abundant in 4 to 6 per cent. glycerin-bouillon, especially in wide-bellied flasks. One must take the precaution, however, of floating the particles used for culture upon the surface of the medium, since if they fall to the bottom they are deprived of air and consequently find an unfavorable condition for development.

Within two to three weeks, if the sowing has been successful, there is a strong, thick, dry pellicle of extraordinarily luxuriant growth, which becomes folded upon itself and even creeps up the side of the glass in a manner entirely unknown in other media. This method is especially to be recommended when one wishes to procure large amounts of a pure culture within a relatively short space of time. On this account it is employed in the preparation of tuberculin. In the preparation of the bouillon one may make use of the meat of various animals—monkeys, horses, dogs, cats, rats, and especially that of the herring (Hippolite Martin), to which glycerin is added. Bonhoff recommended most highly a bouillon prepared from calves' lungs.

Vegetable Media.—In addition to animal media, the tubercle bacilli prosper also upon vegetable matter. For example, avian and mammalian tubercle bacilli flourish upon potatoes kept at body-temperature, if these are kept from drying; the growth being favored by the addition of 5 per cent. glycerin, by access of air, and by a low grade of acidity (Sander). Glycerin-potato-broth has proved a first-class medium; while other vegetable media—carrots, kohlrabi, and macaroni—permit only a limited growth (Sander).

Non-albuminous Media.—The tubercle bacilli have the power of growing upon media entirely free from albumin and peptone, forming their albumin from a mixture composed almost exclusively of inorganic material (Kühne, Proskauer, Beck).

Growth Temperature.—If, on the one hand, the tubercle bacillus evinces a certain adaptability as regards the nutrient media, the range of temperature within which it finds its growth is comparatively narrow. The bacillus of mammalian tuberculosis ceases to grow at a temperature below 29° C. and over 42° C., while that of avian tuberculosis flourishes within the wider range of 25° C. to 45° C. The optimum temperature is 37° to 38°; in avian tuberculosis 39°. Since these relatively high temperatures do not occur, or do not, at least, occur constantly, in the external world, we may deduce the prophylactically important conclusion that tubercle bacilli do not meet with the conditions of growth except solely and exclusively within the animal organism, with its constant and equable temperature of 37° to 39° C. In this regard they differ from other pathogenic forms, notably the bacilli of cholera and of typhoid.

LIFE-PERIOD AND RESISTANCE.

Concerning the life-period and the power of resistance of the tubercle bacilli, there are still, in spite of close investigations on these points, widespread delusions. One finds the most extraordinary descriptions and assertions on the part of certain authors to whom bacteriology seems a rather foreign science. Before their eyes are always the spores of anthrax, endowed with a really unassailable vitality. The wondrous resistance of these forms, once grasped, is attributed likewise to the tubercle bacillus, and conclusions most erroneous, and for prophylaxis and therapy of most critical importance, are deduced therefrom.

There is hardly need of proof that the staining power of the bacilli is not an indication of their vitality, for the bacteria preserve their staining reactions, even after they have been kept in alcohol a decade, or after boiling. So, for example, Wolff, finding that he was able to stain bacilli from an old focus in the lung, concluded positively that they were virulent; and, upon this supposed vitality in a single case built a wild theory of the impossibility of absolute cure.

Life-period in Cultures.—The vitality of the tubercle bacilli does not approach that of other, especially spore-building, bacilli, but is rather narrowly limited. It depends in part on the nutrient medium and seems to be diminished in proportion to the rapidity and luxuriance of growth. Serum cultures last about six months, glycerin-agar cultures are often entirely or in part dead after six or eight weeks, but there are many variations from these rules. The cultures of chicken tuberculosis keep their vegetative and pathogenic characteristics much longer; according to Maffucci, even for several years.

Resistance to Desiccation.—Of great practical importance was the question of how long tubercle bacilli retained their vitality in a dried condition; how long, in other words, did sputum, often expectorated by patients in any and every place and left to dry, retain its infectious qualities. In a large number of investigations, which were occupied with this problem, the vitality and the proliferative capacity of the bacteria was determined by inoculation upon animals.

Schill and Fischer found dried sputum still virulent by the ninety-fifth day, dead by the one hundred and seventy-ninth day. In another case the bacilli were in part dead by the one hundred and eighty-sixth day, and completely gone after the seventh month. Sormani found that sputum dried in thin smears was virulent after two months, harmless after four months; sputum dried upon glass was dead at the end of four months; dried upon cloth was dead after the end of the fourth month, in one case after the sixth month. Toma found dried sputum virulent up to ten months; and Sawitzki found dried sputum lifeless under ordinary conditions after two and one-half months. Maffucci found cultures of avian tuberculosis dried upon silk threads entirely lifeless after two months, while after the same period similar preparations of mammalian disease still retained some vitality.

Cadéac and Malet rubbed up to a powder dried pieces of tubercular lung, and found that after one hundred and two days these had lost their virulence. Another piece of this lung they hung up before the window and permitted it to decompose and dry; only after one hundred and fifty days of exposure did it give negative results with inoculation.

Stone, of Boston, asserts that he observed only a diminution, not an absolute loss, of virulence in a lung which had been dried for three years. As this observation contradicts the experience of many other investigators, and has, to my knowledge, found no confirmation, the suspicion of some blunder in technic cannot be avoided.

The somewhat dissonant results of the various authors are in part explicable by the varying thickness of the smears in which the sputum was allowed to dry, a circumstance of which Sormani had already emphasized the importance. It is also important whether the sputum was kept in the dark or in a diffuse light, or in sunlight, factors concerning which information is mostly lacking in the various articles.

On the whole, one may assume that after about three months dried sputum loses its virulence, but under extraordinary circumstances retains it as long as six or eight months.

Resistance against Decomposition.—The tubercle bacilli last a shorter time in fluid media than they do in a dried condition, since they are deprived of air. Very soon the process of decomposition begins, and exercises a most deleterious and destructive effect upon the tubercle bacilli. Schill and Fischer were able to demonstrate virulent tubercle bacilli in decomposing sputum even after forty-three days.

Galtier succeeded in producing the disease with tuberculous tissues which had been decomposing in water from two weeks to two months. Sormani states that tuberculous sputum preserves its vitality in water more than ten months. On the other hand, Falk, Baumgarten, and Fischer concluded that the virulence of tuberculous material exposed to decomposition was already diminished, sometimes entirely destroyed, even within a few days. According to Toma, the tubercle bacilli maintain their virulence in fluid sputum between eight and eleven days, varying with the degree of decomposition.

The overgrowth and annihilation of the tubercle bacilli by other bacteria has an important bearing on prophylaxis, since the growth of the bacilli outside of the body is thus *à priori* excluded through the universal distribution of the saprophytic forms. As we shall see in the discussion of bacteriotherapy, Cantani attempted to make a therapeutic application of this limited power of resistance.

Resistance to Heat.—The action of heat upon tubercle bacilli has been exhaustively studied. According to Schill and Fischer, they were still alive after an hour's exposure to dry heat at 100° C., whereas in live steam they were partially destroyed after fifteen minutes, and completely so after thirty minutes; while five minutes of boiling annihilated them. Grancher and Ledoux-Lebard reaffirmed the increased power of resistance of the tubercle bacilli to heat. Further investigations upon this subject by Sormani, Yersin, Forster, Bonhoff, Grancher, Ledoux-Lebard and de Man gave the results tabulated on page 45.

With these results agree those of Heim, that tubercle bacilli are killed in sputum kept at 70° C.

The much-quoted experiments of Voelsch, according to which a single or a second boiling of fluids containing the bacilli did not suffice to destroy their virulence, are not conclusive, since the animals (rabbits) were killed on account of lack of time after seventeen days, and since the localized foci with caseous interior, as they were found by Voelsch in these animals, may also be produced, as is well known, by dead bacilli.

To sum up: a temperature of 55° C. kills the bacilli only after acting for about six hours; one of 60° C. in one hour; and one of 90° C. within the space of two minutes; the mammalian bacillus being less resistant, as has been shown by Maffucci, than the avian. Subjection for a very brief period to the action of higher temperatures, as is practised in the Pasteurization of milk, destroys the virulence of the tubercle bacilli only when the temperature approaches boiling-point.

Forster	In milk	95°	1 min.	Sterile for animals.
de Man	" "	90°	2 "	Sterile for animals.
Forster	" "	80°	1 "	Still virulent.
de Man	" "	80°	5 "	Sterile for animals.
Grancher and Ledoux-Lebard	Watery suspensions of cultures of mammalian tuberculosis.	70°	1 "	Sterile for animals and media.
Grancher and Ledoux-Lebard *	Watery suspensions of cultures of avian tuberculosis	70°	1 "	Dead for animals, not for media.
Sormani	Milk with sputum	70°	10 "	Still virulent.
de Man	" " "	70°	10 "	Sterile for animals.
Yersin * †	Tuberculous splenic pulp of avian tuberculosis	70°	10 "	Dead.
Yersin * †	Moist cultures of avian tuberculosis.	70°	10 "	Dead.
Grancher and Ledoux-Lebard *	Watery suspension of avian tuberculosis.	70°	15 "	Sterile for media and animals.
Bonhoff	Bouillon cultures	70°	20 "	Sterile for animals.
Grancher and Ledoux-Lebard	Watery suspensions of mammalian tuberculosis	60°	1 "	Still virulent for animals.
Grancher and Ledoux-Lebard *	Watery suspensions of avian tuberculosis	60°	10 "	Still virulent.
Grancher and Ledoux-Lebard *	Watery suspensions of avian tuberculosis	60°	15 "	"
Bonhoff	In bouillon cultures	60°	20 "	Sterile for animals.
Forster	In milk	60°	45 "	Virulent.
Forster	In sputum	60°	1 hr.	Sterile for animals.
Forster	In milk	55°	3 "	Virulent.
Forster	In sputum	55°	6 "	Sterile for animals.

Resistance to Cold.—The tubercle bacilli have the power of resisting cold for a long period. In Galtier's experiments even temporary freezing did not destroy their virulence. In the winter of 1888 the author allowed some tuberculous sputum to dry upon asphalt plates in the narrow yard of the Institute. In a few days it snowed, and the frost often fell as low as —10° C.; the snow lay for about three weeks. In the fifth week there was a second snowfall, lasting several days. Every week, from the first to the sixth, sputum specimens were taken and inoculated upon guinea-pigs. Every time, even after the sixth week, the sputum was found to be of full virulence. As these investigations were undertaken for a different purpose, accurate temperature records were not kept, yet they suffice to show that tubercle bacilli retain their vitality as long as six weeks at very low temperatures, up to —10° C., under a covering of snow.

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* In these cases the experiments were made with avian tuberculosis, in the others with the mammalian disease.

† Yersin tested vitality only upon artificial media, not upon animals.

Resistance in the Earth.—The tubercle bacillus can maintain itself for some time underground. Particles of lung taken from the body of a tuberculous rabbit buried 0.80 meter underground were still virulent, according to Galtier, after twenty-three days. Cadéac and Malet had positive results from the inoculation of tuberculous lungs after burial for one hundred and sixty-seven days.

Schottelius records that he found still virulent tubercle bacilli in a lung buried for two and one-half years, and even in the surrounding layers of earth, and that he prepared pure cultures (! ?) therefrom. The latter statement seems *à priori* improbable, since at that time no method had been perfected by which it was at all possible to grow tubercle bacilli pure from mixed cultures. According to Petri, tuberculous rabbits buried in zinc coffins were capable of giving rise to infection up to three months and six days; those buried in wooden coffins, up to one month and five days; after longer periods they were found to contain non-virulent bacilli.

Resistance to Sunlight.—It has long been known that the light is injurious to germs. According to Koch, tubercle bacilli die within a period varying from a few minutes to several hours, depending upon the thickness of the layer in which they are exposed to direct sunlight. The same effects result from exposure to diffuse light for an appreciably longer time. Cultures which were put before the window but were protected from the direct rays of the sun perished after five to seven days. Straus determined that flourishing glycerin-bouillon cultures of mammalian and avian tuberculosis, exposed for two hours upon a balcony to the rays of the summer sun, had completely perished. Cultures dried in thin smears upon glass plates had lost their virulence in half an hour under the same conditions. Tubercle bacilli dried upon cloth were injured, according to Migneco, by an exposure of from ten to fifteen minutes to sunlight, and were completely destroyed after twenty-four to thirty hours.

Resistance to Chemicals.—The necessity of rendering tuberculous material, especially sputum, innocuous stimulated thorough investigations into the effects of chemical agents upon the tubercle bacillus. There was, further, a widespread expectation that it might in this way become possible to discover a remedy against the disease. According as the former or the latter of these objects was the more prominent, the experimenter tested his chemicals with sputum, on the one hand, or with pure cultures on the other. The final proof, the test of the experiment, was afforded by inoculation upon animals, at times by the less reliable method of cultivation on dead media. Sublimate, according to Schill and Fischer, was not adapted to the disinfection of sputum, since even a 2 per cent. solution added to an equal quantity of sputum failed to accomplish the purpose, owing to the coagulation of the superficial layers.

Five per cent. carbolic acid to an equal quantity of sputum destroys the germs within twenty-four hours if the fluid be occasionally stirred about; 2.5 per cent. carbolic acid does not accomplish the disinfection of an equal quantity of sputum within twenty-four hours.

Absolute alcohol, added in ten times the quantity to sputum, acts as a certain disinfectant within twenty-four hours.

Tubercle bacilli dried upon blotting-paper were destroyed in twenty-four hours by sulphur fumes, when the sulphur was employed in the proportion of 30 to 40 gm. to every cubic meter of air (Vallin). For the bacilli in sputum and in cultures of chicken tuberculosis it required 60 gm. of sulphur to every cubic meter of air (Thoinot). Smaller quantities of sulphur gave unreliable results.

Various chemicals were thoroughly tested with regard to their disinfectant action upon tubercle bacilli; namely, carbolic acid, boric acid, creosote (Küssner), ethereal oil of eucalyptus, thymol (1:500), watery solutions of creosote (1:200), etc. (Cavagnis), salicylic acid, bromin, creosote, etc. (Parrot and H. Martin), α- and β-naphthol, turpentine, bromethyl, lactic acid, camphor, etc. (Sormani and Brugnatelli.)

Yersin instituted experiments of this kind upon cultures of avian tuberculosis. Paul Villemin tried to determine to what extent the addition of chemicals (of which he tested 114) to the nutritive medium influenced the growth of the tubercle bacilli, either by disturbing their development, or by absolutely inhibiting their vegetative processes, or by sterilizing the medium. Especially active were: Hydrofluoric acid (1: 5000), ammonia, the silicate of fluorin and iron, the silicate of fluorin and calcium, the silicate of fluorin and sodium, α-naphthol, β-naphthol, potassium polysulphid, and copper sulphate.

According to Destrée and Gallemaerts, the growth of tubercle bacilli was inhibited by the addition to glycerin-agar of 4 per cent. sublimate; 4 per cent. iron sulphate; 20 per cent. zinc sulphate; 20 per cent. chlorid of calcium; 20 per cent. turpentine; 20 per cent. potassium permanganate; 8 per cent. potassium soap.

The favorable reports of well-known surgeons, as Mosetig-Moorhof, Mikulicz, Gussenbauer, Verneuil, Terrillon, and later Bruns and Trendelenburg, upon the iodoform treatment of tubercular foci gave occasion to a special investigation of the action of this agent upon tubercle bacilli. Baumgarten, Rovsing and Catrin, were unable to demonstrate its activity experimentally. Gosselin, however, declared that he had noticed a retardation of the tuberculous process in animals after the injection of 10 per cent. iodoform. Ruyter, Behring and Paul Villemin, also, found that iodoform was prejudicial to the growth of tubercle bacilli in cultures. According to Troje and Tangl, tubercle bacilli which had been exposed for a considerable length of time to the action of 15.80 times their own bulk of iodoform produced a rather chronic form of tuberculosis with a tedious course in rabbits, while after an exposure of about three weeks they were entirely destroyed. Any influence of iodoform injections upon experimentally produced abscesses in rabbits could be determined.

Stchégoloff, by the addition of 5 per cent. iodoform to glycerin-bouillon, was able to inhibit the growth of tubercle bacilli; after forty-eight hours the sowing had completely lost the capacity for development, even when transplanted to other media.

According to Koch, there are numerous volatile oils which even in small quantities restrict the growth of tubercle bacilli; among the aromatic compounds, β-naphthylamin, para-toluidin, xylidin, some of the so-called tar-stains, namely, fuchsin, gentian-violet, methylene-blue, chinolin yellow, anilin yellow, auramin; and among the metals, the vapor of mercury, silver and gold compounds. "The cyanide of gold compounds were noteworthy by their surpassing activity in this regard; even in a dilution of 1:2,000,000 they retarded the development of the tubercle bacillus." All of these substances were inactive, however, when tested upon animals. (Koch).

CONCLUSIONS REGARDING BIOLOGY.

Briefly to summarize the biological peculiarities of the tubercle bacillus, we are dealing with a micro-organism which, according to all previous experience, needs for its development a high temperature corresponding about to that of the blood, and which is to be regarded as a true parasite, lacking the conditions necessary to its development externally to the animal body. It is characterized by an extraordinarily slow rate of growth, even when planted upon favorable media and kept at a proper temperature.

Its power of resistance to the deleterious action of external agents gives it in every phase of its existence, whether as simple bacillus or as such with presumable spore-formation, a middle rank between those bacilli which entirely lack spores, and those resistant forms, such as the spores of anthrax or the potato-bacillus (Globig), the tenacity of which it does not even faintly approximate.

It is capable of withstanding high temperature only to a limited extent; even at 70° to 80° C. it dies within a few minutes. It is less susceptible to cold; even when frozen it maintains its proliferative capacity for days and weeks. Sunlight exercises an extremely pernicious influence upon its growth; direct light kills it within a few minutes to a few hours; diffuse light within several days.

When dried in layers not too thin, it is able to prolong its existence from several months to a year. In conflict with other germs,—*e. g.*, saprophytic forms,—in the same nutrient medium, the tubercle bacillus is at a disadvantage from the start by reason of its slow rate of reproduction, is easily crowded out and, as it were, asphyxiated—a further cause of its inefficiency under the conditions of the external world. Numerous chemical substances inhibit its development and destroy its virulence.

In addition to the external influences which hem the existence of the tubercle bacillus within relatively narrow bounds, there are also certain intrinsic factors which appear to exert a similar influence upon its life. Even under favorable conditions, when cultivated upon dead media and at a proper temperature, in spite of being shielded from all deleterious influences, it perishes within a relatively short time (in serum after six months, in glycerin-agar in from four to six weeks); and apparently this process is rapid in proportion to the luxuriance and freedom of its previous growth. Within the human and the animal body the vitality of the tubercle bacillus is similarly rather feeble. The greater number of the bacilli contained in phthisical sputum and in the cavities are, indeed, as has been shown, no longer capable of further growth.

Many of the bacilli situated in the tissues appear to have perished, at least this conclusion is indicated by the difficulty of growing vigorous cultures even from old pieces of tissue infested by the organism.

Löte thought that he had determined a difference between the virulence of freshly grown bacilli and those which had been repeatedly transplanted upon favorable media. Recently Vagedes attempted to demonstrate a variable virulence in the cultures from different sources; these investigations have not as yet, however, yielded any positive results.

[Lartigau * experimented by inoculation with cultures of the tubercle bacillus obtained from different sources. He found well-marked variations in their pathogenic power. Among his conclusions are the following:

The bacilli of great virulence were, on the whole, more difficult to cultivate and their growths were scantier than in the case of bacilli of less virulence. In so-called scrofulous lymphadenitis the bacilli are generally of low virulence. In acute miliary tuberculosis the bacilli may be of great virulence. When tubercle bacilli of great virulence are present in lymphadenitis, the process is apt to spread to other tissues. The tubercle bacilli present in pulmonary tuberculosis with ulceration may be of feeble virulence, especially in those cases in which the clinical history indicates a slowly progressing lesion.

Trudeau, Behring, and others have found that the bacilli that have been cultivated upon artificial media through many generations have gradually lost their pathogenic power, and these are now being widely used in experiments upon artificial immunity.

Krompecher and Zimmerman,† on the other hand, inoculated pure cultures, obtained from thirty cases of surgical tuberculosis, and found that they showed the same virulence as did those from pulmonary cases. They conclude that the essential element in the difference in the rapidity of the disease in various situations is a difference in the resistance of the tissues rather than in the virulence of the bacilli.

Clinical observation tends rather to sustain the claim of Lartigau, but doubtless practically both elements are of importance.—Ed.]

CHEMISTRY OF THE TUBERCLE BACILLUS.

By E. R. Baldwin, M.D.

Chemical investigations of the tuberculous diseased tissues were made soon after the discovery of the bacillus, and exhaustive analyses of the bacillus were made possible by the introduction of glycerin culture-media whereby large quantities of bacilli were easily cultivated. The discovery of the effects of dead bacilli and of tuberculin, together with the search for an antitoxic serum, gave great

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† Centralblatt f. Bact. u. Parasit., Bd. xxxiii, No. 8

impulse to the study; so that more than any other pathogenic bacterium the tubercle bacillus has received especial attention; and the results have served to explain the symptoms and pathology of tuberculosis better than was before possible.

ELEMENTARY COMPOSITION.

Hammerschlag was the first to publish an elementary analysis of tubercle bacilli from broth and agar cultures. The quantity—27.5 gm. (moist)—was relatively small, and later analyses by de Schweinitz, Ruppel, and Levene are of more importance.

It was found by Cramer, with other bacteria, that the elementary composition varied widely according to the medium which supported their growth. de Schweinitz and Levene observed the same fact with respect to the tubercle bacilli.

The employment of various synthetic media composed of salts without peptone or beef extract, by de Schweinitz, Kühne, and Proskauer and Beck, made it possible to illustrate the differences in composition in comparison with broth media. The greatest variation appears in the total ash and phosphorus determinations.

The following tables give the averages from de Schweinitz and Dorset, and comparative analyses by Hammerschlag and Levene, of the fat-freed bacilli on various media:

TABLE I.

de Schweinitz and Dorset.

	Cultures on: Broth.	Cultures on: Asparagin, Synthetic Media.	Cultures on: Broth.	Cultures on: Asparagin, Synthetic Media.
	Dried at 100° C.		Ash-free.	
C	61.55 per cent.	62.16 per cent.	63.33 per cent.	63.35 per cent.
H	8.59 "	9.19 "	8.88 "	9.36 "
N	7.55 "	8.94 "	7.74 "	9.14 "
S	0.44 "	0.22 "	0.45 "	0.23 "
P........	0.82 "	0.66 "	—	—
Ash......	4.03 "	1.92 "	—	—

TABLE II.

	Hammerschlag.	Levene.	
	Cultures: Agar and Broth.	Cultures: Broth.	Cultures: Mannite, Synthetic Media.
Alcohol and ether extract = fat	.27.2 per cent.	31.56 per cent.	22.18 per cent.
C ..	51.62 "	55.58 "	47.41 "
H ..	8.07 "	8.46 "	7.05 "
N .	9.09 "	9.39 "	7.91 "
S ..	—	1.39 "	0.25 "
P...	—	0.59 "	2.67 "
Ash	8.00 "	5.92 "	10.00 "

ASH.

de Schweinitz examined the ash from glycerin-bouillon cultures of attenuated bacilli, with the following result: The ash varied from 2 per cent. to 4 per cent. and contained: Na_2O, 13.62 per cent.; K_2O, 6.35 per cent.; CaO, 12.64 per cent.; MgO, 11.55 per cent.; SiO_2, 0.57 per cent.; P_2O_5, 55.23 per cent. Later determinations of the phosphorus content with bacilli from broth containing acid potassium phosphate gave much higher percentages for the attenuated (74.38 per cent.) than for virulent human (60.90 per cent.) or bovine (58.04 per cent.). The higher content of phosphorus is especially noteworthy, and in general seems to vary with the fat-content of the respective bacilli. Chlorids and sulphates were probably washed out in the preliminary treatment with hot water.

ORGANIC CONSTITUENTS.

The following table gives the estimates by percentages, showing the wide variations due to different methods of analysis or media:

TABLE III.

	Hammerschlag.		de Schweinitz and Dorset.				Ruppel.
			Dried at 100°.		Ash-free.		
			Broth.	Asparagin.	Broth.	Asparagin.	Broth.
Fat	27.2	per cent.	42.33	42.01	43.90	42.87	23.5
Proteid	26.9	"	46.34	55.87	48.10	57.12	31.7
Carbohydrate or other residue	28.1	"	7.16	7.46	4.75	4.84	44.8
Ash	8.0	"	2.90	1.92	—	—	—

PROTEIDS.

Hammerschlag first recognized proteid in the bacillus and ascribed the acid-resistance after staining to a peculiar combination of this with the other substances in the bacillus.

Weyl extracted a mucin-like substance with dilute NaOH, which on account of its toxicity he regarded as chiefly a toxo-mucin. Hoffman also separated various proteids by extraction with water; 1 per cent. HCl; 2 per cent. KOH cold and then hot. Nothing definite as to their nature was, however, known until improved methods of analysis revealed the presence of the nucleic acid combinations known as nucleo-proteids. Kühne and de Schweinitz first noted the presence of such a substance in cultures on synthetic media, and Ruppel simultaneously with Levene published more detailed studies. Ruppel found no coagulable proteid in the water extract of powdered bacilli grown on broth, and the substance gave only the biuret reaction among all the color tests for proteids. Acetic acid gave a marked precipitate, which contained over 4 per cent. of phosphorus. Water dissolved one-half of the pulverized bacillus substance. One per cent. NaOH dissolved 15 per cent. from intact bacilli, while NaCl and weak acids extracted very little. Digestion with pepsin or trypsin also removed but little. All solutions gave remarkably slight proteid reactions and very little coagulable proteid or ordinary albumin. Weyl's toxomucin was thus identical with the nucleo-proteid. Ruppel suggests that the small amount of coagulable proteid may be due to the self-coagulating action of the free nucleic acid formed in growing cultures. The residue from extracted bacilli was mainly chitin or a keratin-like substance.

Levene, using extracts of pulverized bacilli from asparagin and mannite cultures by means of 8 per cent. NH_4Cl, found three nucleo-proteids having different heat coagulation points and solubilities: (1) Coagulated at 50° to 64° C. can be precipitated by 50 per cent. $MgSO_4$ or saturated NaCl; (2) coagulated at 72° to 75° C. can be precipitated by saturated $MgSO_4$; (3) coagulated at 94° to 95° C. can be precipitated by saturated $(NH_4)_2SO_4$. All three contained phosphorus; the third more than the first two.

Levene found no ordinary albumin in the extracts of bacilli, the body-substance consisting principally of nucleo-proteids. Therefore the presence of true toxalbumins analogous to those of other bacteria—diphtheria, cholera, etc.—has not been demonstrated in extracts of tubercle bacilli.

The proteids of tuberculin and the decomposition products of the nucleo-proteids are described under their respective titles. The physiological action of these and other products of tubercle bacilli is considered under a separate heading.

CARBOHYDRATES.

Freund, Dreyfus, and Nishimura made successful tests for carbohydrates in tuberculous tissues which they regarded as proof of the presence of cellulose in the bacilli. Hammerschlag and de Schweinitz and Dorset obtained similar results from cultures. Nishimura and Weyl failed to detect by Fehling's copper test any evidence of carbohydrate, though the latter found a mucin-like body which did not reduce copper oxid. Ruppel ascribed these results to the decomposition of the chitin substance, which resists nearly all extraction but slowly dissolves in concentrated HCl. Its solution reduces alkaline CuO. No carbohydrate was detected by him. Bendix found a pentose in combination with the nucleo-proteid of the bacillus which could be separated by heating pulverized bacilli with 5 per cent. HCl. He identified it by chemical and spectroscopic tests.

Levene isolated a glycogen-like substance from the sodium chlorid and ammonium chlorid extracts of pulverized bacilli, and also from the residue after extraction of the bacilli by these salts. He isolated it by precipitation, together with the nucleic acid from which it is separated by $CuCl_3$. Chemical reactions identified it as glycogen. It did not reduce CuO unless heated with acids, but gave a characteristic color with iodin. The tubercle bacillus thus would appear to contain a carbohydrate more nearly allied to the sugars than cellulose, but in close combination with the nucleic acid. On the other hand, it does not seem demonstrated that cellulose is absent by any analyses thus far made.

FATS.

The fat or wax ingredients of the tubercle bacilli are very remarkable and important. They form from 10 per cent. to 40 per cent. of their substance, and are difficult to entirely remove by extraction. No other known bacterium contains so much fat, the greatest amount being about 10 per cent. in the bacillus of multiple gangrene (Bovét). The acid resistance is largely, if not entirely, due to the peculiar quality or combination of the fat in the body-substance of tubercle bacilli. Hammerschlag found an average of 27.2 per cent. alcohol and ether extract of agar and yeast broth cultures, which he thought to contain lecithin, tri-palmitic, and tri-stearic acids. de Schweinitz and Dorset, Aronson, Ruppel, and Kresling have made the most extensive examinations of the fats, employing very large quantities of bacilli for the purpose.

de Schweinitz and Dorset with bacilli grown on media rich in phosphates,—7 per cent. glycerin,—heated and washed with hot water, found as high as 37 per cent. to 42 per cent. fat, which from the melting-points and solubilities was thought to consist of the fatty acids, palmitic, arachidic, and possibly lauric. A minute quantity of volatile acid gives the characteristic almond odor to cultures. Aronson prepared 70 gm. of fat, 17 per cent. of which was free fatty acid, the residue being wax, much of which was not easily saponified; was soluble in ether or dissolved on heating with acetic anhydrid like an alcohol, but of different nature from cholesterin. Aronson observed that by low percentages of glycerin in the media the wax is much less. Ruppel found the fat percentage to vary, according to the age of the cultures, from a minimum of 8 per cent. to 10 per cent. to a maximum of 25 per cent. to 26 per cent. He used 2 per cent. broth cultures. He distinguished three varieties of fats, as follows: (1) Soluble in cold alcohol, consisting of free fatty acids and glycerin; (2) soluble in hot alcohol; probably palmitic and stearic acid-esters of some higher alcohols; (3) soluble in ether; also containing fatty acid-esters, probably of ceryl and myricil alcohols.

Kresling used broth cultures heated to 110° C., washed, dried, and pulverized. He found from 25 per cent. to 40 per cent. of fat, according to the solvents used. The largest amount was obtained from the chloroform extract (35.72 per cent. to 36 per cent.). Benzol, ether, and alcohol dissolved less, in the order named. The distillate from the chloroform extract gave the odor characteristic of the bacilli; the free fatty acids comprised 14.38 per cent.; the neutral fat and fatty acid-esters, 77.25 per cent. of the extract. He recognized butyric acid, cholesterin; and from the ash analyses, on account of the large content of phosphorus, estimated 16 per cent. of lecithin in the fat. According to Kresling, the tubercle bacillus fat consists of a mixture peculiar to itself and unlike any other known fat or wax. It contains free fatty acids, neutral fat, fatty acid-esters, and higher alcohols (lecithin and cholesterin), besides a large amount (25.76 per cent. of the total fat) of other extractives insoluble in water. These latter partly decompose by heating with alkalies into products soluble in water.

The study of the fat made by Proskauer with Koch led them to think that it formed a protecting layer about the bacillus and contained two fatty acids. Both were acid resistant when stained. Alcohol dissolved one, but fixed the dyes in the other. Klebs, Unna, Aronson, and Levene also ascribe the acid resistance to the fat or wax in the bacillus.*

The wide variations in the percentage of fat found by different authors may be explained by differences in the amount of glycerin and phosphates in the media and the methods used in preparing the bacilli for extraction. The differences due to media and origin of bacilli are considered under Bio-chemistry (page 57).

* On the ground that chitin in the ova of tænia was found accidentally to resist acid after staining, by Helbing, he regards the acid resistance of tubercle bacilli as explained in the same way. The ova had been the cause of a tubercle-like growth in the omentum. A further support to this idea was the belief by Ruppel that chitin was a normal ingredient of the bacilli. It may be possible that the fat and chitin both have this property.

OTHER EXTRACTIVES AND DECOMPOSITION PRODUCTS.

Alkaloids or Ptomains.—Zuelzer, Héricourt and Richet, Crookshank and Herroun have detected poisons of this nature in acid and alcohol extracts of bacilli or cultures, but later research has not confirmed their presence. On the contrary, the toxic principles appear to be of an acid nature. A few years later de Schweinitz isolated an acid substance of crystalline nature, which was soluble in ether, alcohol, and water, and on analysis had a formula resembling teraconic acid, one of the fatty acids. It appeared to have necrotizing properties on the liver of guinea-pigs.

Nucleic Acid or "Tuberculinic" Acid.—Ruppel isolated free nucleic acid from the filtrate after precipitation of the nucleo-proteid by acetic acid from the watery extract of pulverized tubercle bacilli. This can be precipitated by alcohol and has the highest degree of toxicity of any substance thus far isolated from tubercle bacilli. Analyses by Ruppel gave from 9 per cent. to 9.4 per cent. phosphorus.

Levene analyzed the tuberculinic acid obtained both free in extracts of tubercle bacilli and from the nucleo-proteid. The average composition was: C, 33.66 per cent.; H, 5.83 per cent.; N, 9.62 per cent.; P, 11.33 per cent.

On decomposition by heat on a water-bath a series of products were found by Ruppel some of which, being soluble in alcohol, were recognized as alloxur bases (guanin, xanthin, and adenin). The remainder was a phosphorus-containing acid and related to thymin, which by heating to 150° C. under pressure gave a neutral substance after separating the phosphoric acid. This could be isolated in crystalline form, and was called "tuberculosin." Ruppel considers it the ultimate substance in the tubercle bacilli, without which the characteristic tuberculin action cannot take place.

Levene has discovered more recently thymin and cytosin in the tuberculinic acid. It does not appear whether the latter is identical with "tuberculosin" or not.

The nucleo-proteid or nuclein precipitated by acetic acid gave on decomposition with 1 per cent. H_2SO_4 and purification, a basic substance of protamin character, which was named "tuberculosamin" by Ruppel. The tuberculinic acid is combined with this base in the nuclein.

Kitajima regards the nucleus of the tubercle bacillus poisons as thymin or a similar substance.

It is at present apparent that the complex tuberculinic acid and the more complex nuclein are highly important and characteristic derivatives of tubercle bacilli. This toxin is unique among bacterial products in its resistance to physical and chemical agencies. It withstands boiling, alcohol, acids, and alkalies without losing much of its toxicity.

The results of the foregoing analyses indicate that the relative amounts of substance derived from tubercle bacilli may vary according to the composition and reaction of the culture-medium, age of cultures, and race of bacilli.

Differences in methods of manipulation doubtless account for many quantitative variations in the results given by various authors, and especially when the effects of maceration or heating the bacilli in the culture-fluid are taken into account.

BIO-CHEMISTRY.

ELEMENTS REQUIRED FOR GROWTH.

The great variety of media suitable for the growth of tubercle bacilli has been already considered (see Biology, page 38). Besides oxygen, the importance of glycerin was early recognized, and no carbohydrate was found, in the extensive trials made by Proskauer and Beck, that was a satisfactory substitute for it, although several sugars and starches are able to furnish these elements. The growths are nevertheless limited and slower without glycerin, and from 1.5 per cent. to 7 per cent. of the latter is requisite for vigorous cultures. In the usual 5 per cent. broth cultivation much glycerin remains unused, but less than 2 per cent. is of slight value. Phosphorus in its neutral or acid salts or organic combinations is also essential, and probably most important, considering the large percentage found in the bacillus. By the method of exclusion Proskauer and Beck were finally able to produce good growths on a solution containing only ammonium carbonate, potassium acid-phosphate, magnesium sulphate, and glycerin. From this it was shown that sodium chlorid and complex nitrogenous substances were unnecessary for the support of the tubercle bacillus. By other combinations of salts, potassium was also dispensed with. Nitrogenous components in the medium are, however, indispensable. The nitrogen of the air is therefore not utilized, while a limited supply of oxygen suffices from the same source.

Doubtless vegetable culture-media are favorable because they contain phosphates and carbohydrates in abundance; while brain infusions furnish phosphorus in organic combinations readily assimilated by the bacillus, thus accounting for its rapid multiplication on such media. An interesting characteristic is its tolerance of a high degree of acidity due to acid salts or its own metabolic products in cultures. When the acidity is due to acid potassium phosphate, the growth is even markedly promoted when gradually habituated to it in transplanting from one culture to another. de Schweinitz and Dorset find the virulence of tubercle bacilli is conserved by the substitution of acid potassium phosphate for sodium chlorid in media. It is doubtful whether acidity as such favors virulence, since alkaline blood-serum is well known to be very suitable for this purpose. On the other hand, Ficker suggests that increased acidity of mucus in the bronchi is a possible factor favoring the growth of bacilli in the sputum.

PRODUCTS OF GROWTH.

Volatile Fatty Acid.—During the active multiplication of tubercle bacilli on liquid media an odor of characteristic nature is developed resembling that of violets or almonds. This is ascribed to a volatile fatty acid, and is found in the alcoholic extract, but has not thus far been identified.

Pigment.—There is also a lemon-yellow color with well-marked fluorescence developed in the liquid, easily seen in full-grown cultures on synthetic media. The pigment changes to a faint brown in solutions on prolonged exposure to light or heating, and can be partially extracted from the bacilli by salt solutions. It is very soluble in alcohol, a drop of this solution producing marked fluorescence in water (Levene).

Owing to the dark red color developed in the bacilli or the fat residue from alcohol on exposure to the air, Ruppel considers that it exists as a chromogen in the bacillus and not as a preformed pigment. It is probably closely associated with the fatty acids.

Alkaloids.—Reference has already been made (page 56) to the alkaloids and ptomains described by Zuelzer, Héricourt and Richet, and Crookshank and Herroun as excretions of tubercle bacilli. Confirmation of their presence has not been forthcoming from later studies.

Toxalbumins.—The so-called toxalbumins or toxalbumoses of Hammerschlag, Klebs, and Maragliano correspond to the heat-coagulable nucleo-proteids found by Levene extracted from the bacilli and present to some extent in the culture filtrates. There is, however, no evidence that they are true secretions or excretions of the bacilli, being more likely due to the maceration of dead or old bacilli and their consequent extraction.

There is very little proteid dissolved out or secreted in actively growing cultures on synthetic media, and no differences in this respect have been detected in the products from broth media.

de Schweinitz was able to isolate an acid (see page 56) from the synthetic cultures, but not readily from the broth filtrate. He thought the acid may have been combined with the bases of the meat extract present. Aronson considered the fat of tubercle bacilli as a secretion which collects between them, while Ruppel suggests that the nucleic acid formed by the bacilli, if in excess, coagulates the proteid substance, thus accounting for the small amount of proteid in watery extracts. This may also account for the small amount in culture filtrates.

Ferments.—Kühne concluded because of the presence of certain albumoses and so-called "tryptophan" in tuberculin that a proteolytic action was produced by the bacilli.

Hahn found that the plasmatic juice squeezed from living bacilli by hydraulic pressure decomposed H_2O_2, a reaction said to be characteristic of enzymes.

Marpman detected a trace of PH_3 gas by its chemical reaction on silver. No further evidence has been adduced as to ferment action.

Differences in Products.—de Schweinitz and Dorset by comparative estimations of the fats from bacilli of different origin and virulence found the largest percentage (37.41 per cent.) in the attenuated human bacilli. The virulent human (28.03 per cent.) and bovine (26.32 per cent.) bacilli were more nearly alike.

Acidity.—Estimations of the free acids contained in the fats by de Schweinitz and Dorset showed similar relations between the attenuated human and bovine, but the virulent human was nearer the attenuated in having a larger content of acid.

Smith has shown that the reaction of cultures varies according to whether they are of human or bovine origin.

The human cultures, at first acid to phenol-phthalein, became less so; but when the growth was nearly complete they increased in acidity, finally exceeding the original degree. On the other hand, the bovine cultures decreased in acidity, at times beyond the neutral point, and remained feebly alkaline. In cultures containing no glycerin no differences were noted; both decreased in acidity and passed the neutral point.

The coincidence between the greater percentage of free fatty acids in human bacilli as found by de Schweinitz and Dorset and the greater acidity of glycerin broth cultures is certainly significant. Since glycerin was found essential to this difference in the reaction of cultures it is fair to assume a larger amount of fatty acids produced by human than by bovine bacilli as the cause. The preliminary decrease in acidity in both may be accounted for by the removal of acid salts utilized by the multiplying bacilli before the fatty acids are formed or soaked out of them by maceration and age.

PHYSIOLOGICAL ACTION.

The effects of tubercle bacilli and their derivatives on animals have been exhaustively studied, and with notable results.

The local action on the tissues being the object of greatest interest, numerous experiments designed to explain the action of dead bacilli were performed. Most observers failed to produce caseated tubercles, and consequently attributed that phenomenon to the evolution of some irritant, acting in a nascent condition during the life-history of the bacillus.

Effect of the Fats.—Auclair found that the fatty substances extracted from dead human bacilli by ether, benzine, or chloroform produced cheesy abscesses when emulsions in water were injected subcutaneously. The "etherine" or "ethero-bacilline" extract produced caseous pneumonia, and that from chloroform the interstitial form, when injected intratracheally into rabbits. He therefore attributed the caseation to the fatty elements in tubercle bacilli. Levene and Kinghorn produced localized nodules in the peritoneum, and subcutaneously cold abscesses, with combined ether, benzine, and alcohol extracts. Camus and Pagniez found the "etherine" of Auclair destructive to red corpuscles, and Bernard and Salomon by injections directly into the kidney parenchyma found that the chloroform extract, or "chloroform bacilline," caused local cell infiltration, but rarely caseation.

Armand-Delille also produced fibrous lesions in the meninges by the chloroform and ether extracts, but not caseation.

On the whole, the proof is defective that the fat extracted from the dead bacilli can alone cause the coagulation necrosis produced by the living bacillus.

Nearly all observers have failed to note any general disturbances following injections of the fats except in excessive doses, which may produce emaciation, according to Auclair.

Volatile Products.—Auclair worked with the distillate from bouillon cultures, and states that it produced the effects of tuberculin. The same author records an interesting observation as to the danger in working with the ethereal extract of the bacilli. Eight of his colleagues working in the same room suffered more or less violent symptoms resembling a tuberculin reaction within twenty-four to sixty hours after exposure to the vapor. The accidents were attributed to some volatile poison set free in the filtration or evaporation of the ether. None of the individuals affected were suspected of having latent tuberculosis. Similar experiences by others have not been noted, nor in later researches have tuberculin effects been produced by the substances soluble in alcohol, ether, or other fat solvents, except glycerin.

Carriere experimented with the distillate from cultures and ethereal or xylol extracts. Parent guinea-pigs bore dead or weak progeny after repeated injections of these.

The acid substance isolated by de Schweinitz produced lowering of temperature in guinea-pigs and necrosis in the liver when injected directly into its substance. The possible connection which this substance has with the caseation of tubercles has not yet been fully established.

Liquid Culture Filtrates.—The unheated filtrate from broth cultures produces moderate tuberculin reactions, according to most observers.

Maragliano finds that this filtrate evaporated at room-temperature produces a fall of temperature in healthy or tuberculous animals. Bezançon and Gouget and Fraenkel and Bronstein confirm this observation, but Ledoux-Lebard finds only a preliminary fall of temperature, followed by a rise.

The physiological action of the mixture of peptone, glycerin, and beef extracts contained in the broth is to be remembered in these experiments, for it is quite similar. Experiments with filtrates from synthetic media are open to the same objection, but the proteids can be precipitated by saturation with $(NH_4)_2SO_4$ without coagulating them and thus collected in a comparatively pure form. When redissolved in water, the solutions produce mild reactions in no way distinguishable from the effect of ordinary tuberculin.

Nuclein and Derivatives.—Of all the products of tubercle bacilli, the peculiar nucleo-proteid and its derivatives are the most marked in their physiological effects. French and Italian investigators have devoted much attention to the poisonous action of dead bacilli and their extracts, aside from their local action.

Maffucci was among the first to note the cachexia and grave constitutional symptoms of slow poisoning from injections of large quantities of dead bacilli. General atrophy of the viscera and cold abscesses at the site of inoculation were the characteristic lesions found. Chronic nephritis was also frequently observed.

Pansini considered dead bacilli more toxic than living, and Bâbes and Proca concluded that the toxin was set free only after the death of the bacilli.

Experiments with boiled cultures and glycerin extracts of tubercle bacilli by Koch, Hueppe and Scholl, Bujwid, Richet, Trudeau, and others showed that toxin was dissolved by heat which produced the same constitutional effects, but more rapidly than dead bacilli.

Maragliano also prepared a watery extract of the bacilli by heating them three or four days on a water-bath. It had a strong tuberculin activity. The active substance in all these so-called "tuberculins" has been identified by recent chemical and physiological researches as the complex nuclein or its components, analyzed by Ruppel and Levene (page 56).

Sound guinea-pigs bear quite large doses of the nuclein in the form of concentrated water extract of the bacilli, without immediate harm when given subcutaneously. Larger doses produce death in young guinea-pigs after twelve to forty-eight hours, with symptoms of gradual collapse. No lesions except congestion at the site of injection are to be seen. If they survive longer or repeated large doses are given, cachectic symptoms develop.

Behring, in testing nucleic acids from other sources in comparison with tuberculinic acid in the purest form obtainable, noted no special differences in their effect on sound animals, but on tuberculous guinea-pigs and cattle they were 100 times weaker than tuberculinic acid.

The effect of the nuclein or tuberculinic acid on tuberculous animals is to produce a typical tuberculin reaction with local congestion or extravasation of blood about the tuberculous foci. The general reaction is severe, and death occurs in consequence of small doses. Ruppel obtained these effects from several decomposition products, and concludes that the specific toxicity rests with the thymin-acid nucleus—named "tuberculosin."

The relative toxicity of various preparations was measured by the fatal dose for four to six weeks' tuberculous guinea-pigs killed by one gram of acid or other product subcutaneously administered. Some of these are given by Behring and Ruppel, as follows:

Ordinary tuberculin	1 gm.	= 2,000 gm.	tuberculous	guinea-pigs.
Precipitated tuberculin	1 gm.	= 40,000 "	"	"
Pulverized tubercle bacilli	1 gm.	= 40,000 "	"	"
Tubercle bacilli nuclein	1 gm.	= 60,000 "	"	"
Tuberculinic acid	1 gm.	= 70,000 "	"	"

No greater degrees of toxicity were found in "tuberculosin" or "tuberculosamin" in proportion to their weight; hence Ruppel regards greater complexity as a condition more favorable to activity; or they are weakened by the process of isolation.

Behring gives the following ratio for the most active tuberculinic acid, according to the methods of injection:

1 gm. =	600 gm.	sound	guinea-pigs	subcutaneously.
1 gm. =	90,000 gm.	"	"	intracerebrally.
1 gm. =	60,000 gm.	tuberculous	guinea-pigs	subcutaneously.
1 gm. =	40,000,000 gm.	"	"	intracerebrally.

Von Lingelsheim and Borrel also employed intracerebral injections of other tuberculins with rapidly fatal effects; tuberculous guinea-pigs being much more susceptible than healthy animals.

de Giaxa prepared nucleic acid from the tubercle bacilli which produced, locally, coagulation necrosis like that in tuberculous lesions. Intravenously it caused thrombi and sudden death. Gioffreddi experimented with the same with similar results. 0.02 to 0.08 gm. intravenously killed rabbits at once from emboli caused by the coagulating action of the nucleic acid on the serum. Evidence has been presented (Badano) that the watery extract of the bacilli can produce caseous pneumonia in rabbits by endopulmonary injections. Dogs, however, only develop transient catarrhal pneumonia from the same, and the experiments hardly apply in explanation of the caseation in actual disease.

Toxins in the Blood and Tissues.—Villa and Maragliano find toxin in the blood and urine of human consumptives who have symptoms of toxemia or tuberculous cachexia. The blood and urine, or extracts of the same, produced tuberculin effects. The human serum killed rabbits by intravenous injection in much smaller doses than that from healthy persons.

Crookshank and Herroun and Maksutow extracted poisonous substances from the tuberculous tissues of guinea-pigs and other animals; on the other hand, Rosa was unable to do so. Mathes found albumoses in tuberculous lymph-nodes and Lenoir a tuberculin-like substance in the urine.

Raybaud and Hawthorn reported hemolytic effects of tubercle bacilli on the red corpuscles of guinea-pigs and rabbits.

Further study is needed to clear up the question of caseation satisfactorily. Leredde and Le Count contribute evidence that caseation may occur in the liver and spleen from circulating poisons, with progressive tuberculosis elsewhere without the presence of the bacilli in the necrosed foci. The amyloid degeneration and interstitial nephritis of this disease are less clearly specific in their origin, occurring during a stage when complicating bacteria are usually present.

The presence of nucleic acid products in the circulating blood may fairly be taken as accounting best for the symptoms and toxemia of tuberculosis; while the intimate combination between the nuclein and waxy substance, which is of itself so difficult of absorption, makes it possible to understand the tubercle formation and the insidiously slow poisoning of this disease.

TUBERCULIN.

CHEMICAL ANALYSES.

Elementary Composition.—R. Koch,* Proskauer and Brieger analyzed two samples of crude tuberculin and one of the precipitated or purified variety. They contained an average of 18.86 per cent. ash, which consisted chiefly of potassium and magnesium phosphate. No chlorin was found. One sample of ash contained 59.84 per cent. PO_3. The average composition of the three samples was: C, 47.82 per cent.; H, 7.26 per cent.; N, 14.85 per cent.; S, 1.15 per cent.

Proteid.—Tuberculin gave all the proteid reactions, but differed from albumoses previously known, also from toxalbumins, by resistance to heat. It resisted 160° C. for two hours in 50 per cent. glycerin solution without apparent weakening. Precipitated tuberculin lost activity when taken up in water, and by further heating on a water-bath gradually became insoluble. Sixty per cent. alcohol precipitated more of the active substance than any other proportion; higher percentages of alcohol brought down more of the proteids from the culture-medium.

Analyses were also made by Heuppe and Scholl, Klebs, Hahn, Hunter, and Kühne. Klebs and Hunter described alkaloids present in tuberculin, but Kühne, who made the most thorough examination, did not find them. The latter found: (1) An albuminate (nucleo-proteid); (2) a peculiar (acro-) albumose; (3) deutero-albumose; (4) traces of peptone; (5) tryptophan, a digestive product. Compared with evaporated broth that had no bacilli grown upon it, there was less albuminate precipitable by 2 per cent. acetic acid and more proteid precipitable by 60 per cent. alcohol in tuberculin. The acroalbumose was found in the broth and the other albumoses were also present, so that only quantitative differences could be discovered between tuberculin and the unused culture-medium. He concluded that the bacilli used or transformed the albuminate into albumoses, and because all the products gave tuberculin reactions none were characteristic. The active substance was, therefore, only attached to them. By cultures on albumose-free peptone and wholly proteid-free media Kühne found an albuminate and albumose in the first but only a trace of albuminate in the latter filtrate. All the products gave tuberculin reactions, and no more definite conclusions resulted as to the nature of tuberculin.

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* Deutsche med. Woch., 1891, p. 1190.

The filtrates from cultures on synthetic media of various composition tried by Proskauer and Beck likewise all caused tuberculin reactions.

The examination by Ruppel of broth filtrates evaporated at 30° to 40° C. instead of boiling heat did not lead to the identification of any specific substance differing in chemical reactions from the proteids in the original broth.

Nuclein.—Nevertheless the nucleo-proteids and tuberculinic acid dissolved out of the bacilli by water, glycerin water 3 to 5 per cent., or weak alkaline solutions proved to contain the active principle to a marked degree, as already described (page 62).

That this active substance was probably in proteid combination in crude tuberculin was recognized by Baldwin and Levene and Nitta. By tryptic digestion of precipitated tuberculin the activity was destroyed, while peptic digestion weakened it.

Ruppel discovered that the active substance was not easily dialyzable either in the form of tuberculinic acid or "tuberculosin." By dialysis he could obtain a fairly pure tuberculin because the glycerin, salts, and albumoses of the broth pass through more easily. The most practicable concentrated tuberculin, according to Ruppel, is that precipitated by 66 per cent. alcohol.

Activity.—Variations in strength were observed by Dönitz in the tests upon tuberculous guinea-pigs. The fatal dose was from 0.100 to 0.35 cc.

Ruppel obtained the impression that the strength of toxins obtained from bovine bacilli exceeded that of human, while the avian produced a yet weaker one.

Owing to the method of preparation of crude tuberculin by boiling the cultures, varying amounts of nuclein would naturally be extracted, and the more alkaline reaction of bovine cultures (Smith) increases the amount dissolved from bovine bacilli.

Tuberculocidin and Antiphthisin (Klebs).—Kühne found traces of deutero-albumose in tuberculocidin, and Trudeau and Baldwin were able to recognize a similar albumose residue from uninoculated broth as well as from tuberculin after the precipitation methods employed in the preparation of antiphthisin. It necessarily contains but a slight amount of active substance.

Tuberculoplasmin (Hahn).—This form of tuberculin contains the nucleo-proteids soluble in water and squeezed out of the bacilli by hydraulic pressure.

Oxytuberculin (Hirschfelder).—Tuberculin weakened by prolonged boiling with H_2O_2, which presumably oxidizes the nuclein into simpler compounds.

Tuberculin "R" (Koch) contains substances remaining after extracting pulverized living bacilli with water. It contains an emulsion of the body-substance in 20 per cent. glycerin, a certain amount being in solution.

Water Extract (Maragliano—von Ruck) contains nuclein and possibly decomposition products of tuberculinic acid and fatty acids.

Tuberculol (Landmann) contains a mixture of normal saline and glycerin extracts of pulverized tubercle bacilli, separately prepared at the temperatures of 40°, 50°, 100° C., then combined and evaporated to small volume at 37° C. It is highly toxic, 0.1 cc. being fatal to a 250 gm. sound guinea-pig.

"Bacillen-emulsion" (Koch) contains the living bacillus substance pulverized and suspended in 20 per cent. glycerin. It presumably contains more nuclein in solution than tuberculin "R".

PHYSIOLOGICAL ACTION—ON MAN.

In Health.—The effect of small doses, 0.001 to 0.010 gm. subcutaneously,* in healthy human beings is inappreciable by any general

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* **Other Methods of Administration.**—*Intravenous.*—Tuberculin produces more marked and earlier reactions when thus administered. The dose compared with the subcutaneous method is only one-tenth as much of the "bacillen-emulsion" employed by Koch.

Ingestion.—Experiences which have been reported on the effect of the old symptoms. At the site of injection local irritation is sometimes produced, resulting in redness and urticarial-like swelling, which is somewhat painful, but quickly subsides. Larger doses, 0.010 to 0.200 gm., may cause temperature elevations from 2° to 4° C. (3.6° to 7.2° F.) in presumably healthy individuals, accompanied by a corresponding increase in pulse-rate, chills, tightness in the chest, cough, headache, vomiting, and muscular pains. These symptoms begin from four to eight hours after the injection, reach their height in two or three hours, then rapidly subside with sweating. In twenty-four hours recovery is complete.

In Disease.—Identical symptoms more or less severe ensue in persons harboring latent or active tuberculosis from much smaller doses, 0.001 to 0.005 gm. By subcutaneous doses of 0.005 to 0.010 of the old tuberculin given to advanced tuberculous patients during the days of reckless experimentation dangerous collapse and even deaths were produced.

Local Reaction.—Tuberculous ulcerations, as in lupus or in tuberculous laryngitis, are readily seen to become deeply red, swollen in their borders, and painful. Tuberculous lymph-nodes or joints become swollen and sensitive to the touch. The local reaction is not so readily recognized in pulmonary or other visceral tuberculosis unless violent reactions are produced.

There is an increased dulness over the affected area of lung and development of crepitant râles when the reaction occurs in areas of considerable extent, while the patient may complain of soreness and the cough and expectoration may increase.

Variations.—With small, old or quiescent foci in the lung or elsewhere considerable fever may result from a small dose without evidence of local reaction; or, on the contrary, all the reaction symptoms may be very mild or even absent. In very advanced, chronic and cachectic stages of tuberculosis, or with calcified tubercles, neither general not local disturbances may result from moderate doses.

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tuberculin when swallowed (Koch) have indicated that considerable amounts can be ingested without symptoms in healthy subjects.

Inunction.—Unna was able to produce local and general reactions in lupus by rubbing an ointment containing 10 per cent. of the original tuberculin into the skin. Spengler also administered the tuberculin "R" by inunctions.

Inhalation.—Tuberculin in its dry form, either as purified tuberculin or pulverized bacilli, may be absorbed from the nasal mucous membrane and produce marked reactions in tuberculous subjects. (Studies from Saranac Laboratory.)

In Other Diseases.—Of still greater importance in diagnostic use is the observation that reactions occur in individuals suffering from other diseases than tuberculosis, notably syphilis. Post-mortem evidence of the absence of latent tuberculosis has not accompanied such reports, as a rule. Healed tubercles are known to react, though usually a larger dose is required. In a large series (2500 cases) of tests made by Beck when other evidence of tuberculosis was wanting there were 54 per cent. of positive reactions, even less than some estimates as to the frequency of latent tuberculosis found post mortem. The majority of these (2137 cases) were convalescent from other diseases not suspected of being tuberculous. Of 143 syphilitics, only 59 reacted (41.25 per cent.).

EFFECT ON THE BLOOD.

Tuberculin causes dilation of the blood-vessels and extravasation of blood about the tubercles when large doses are given. There is also an accumulation of leucocytes and multiplication of connective-tissue cells in the periphery of tubercles, accompanying the dilation of arteries and capillaries. General leucocytosis accompanies the fever reaction with an increased percentage of amphophiles corresponding to a decreased percentage of lymphocytes in rabbits (Kinghorn). The lymph-flow is increased (Roemer and Gärtner), and tuberculin is also positive-chemotactic.

Hulot and Raymond found in rabbits an increase in both white and red corpuscles under the influence of tuberculin after the first injections. Later a decrease in erythrocytes ensued with corresponding anemic symptoms.

EFFECT ON THE TISSUES.

Tuberculin acts as a stimulant to cell proliferation in moderate doses, and by repeated large doses may give rise to connective-tissue growth not only about tuberculous foci but elsewhere. Endarteritis and periarteritis are described by Carrière and others.

Degeneration of kidney epithelium, inflammation of the glomeruli, and fatty degeneration of liver-cells followed by fibrous changes or atrophy are also observed with large doses, especially when given intravenously in animals.

The many researches that have been made both on healthy and tuberculous animals indicate that the effect of tuberculin is in the main identical with that of the toxin produced or set free during the progress of the disease itself. The immediate and remote effects on the tissues and viscera not the seat of actual tubercles are quite the same when the poisoning is prolonged and severe.

The differences in the local action in or around the tubercles are more difficult to explain, and many theories have been put forth to account for the specific reactive phenomena due to tuberculin.*

THEORIES OF THE REACTION.

It cannot be confidently stated that the tuberculin reaction has been fully explained by any of the theories yet propounded. The earlier writers on the subject had the disadvantage of a much less knowledge of the mechanism of immunity in general, which in recent years has aided in the understanding of this almost unique manifestation. Koch first promulgated the idea that tuberculin caused the death of the cells composing the tubercles. Gamaléia held to a like opinion. Buchner, noting that other bacterial toxins caused a reaction, presumed a condition of "latent fever irritability" to exist in tuberculous subjects. Hueppe saw in it only the normal disease process freshly excited by tuberculin. The theory of Charrin also ascribed the reaction to an additional amount of toxin affecting the nervous system. This "additional" explanation has recently been offered by Tinker, who suggests that the reaction is marked only when the patient already suffers slight poisoning from the presence of the disease. Hertwig and Liebmann assumed that chemotaxis explains the local reaction. Arloing thought that the tubercle was weakened by tuberculin, and the poison thus escaping caused the general reaction.

Kohler and Westphal held that tuberculin, being different from the products of the bacilli in the animal, forms a new compound with them which irritates the tubercles. Eber believed in a "heightened cell-energy" which being present in tuberculous subjects and not in normal individuals accounted for the transformation of the tuberculin into "tuberculopyrin" in the former.

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* *Physiological Action of the Broth Constituents.*—It is needful to consider what differences may exist between the action of the pure nuclein and tuberculinic acid, constituting its active principle, and the crude tuberculin in ordinary use. The opinion was early expressed by Hunter that the salts and extractives, partly from the meat extract, caused the fever, while the local inflammatory reaction was specific. On the other hand, the work of Krehl and Mathes established the fact that the albumoses present in the commercial peptone produced well-marked fever and even local reactions in tuberculous animals. Glycerin is also a factor to be included in estimating the effect of large doses of tuberculin. It can, nevertheless, be stated that in actual observations no importance can be attributed to the effect of the broth constituents, except in animal experiments. They may increase or supplement the fever reaction when large doses are being administered, but in the diagnostic use of tuberculin the dose is too small to make them a factor in human practice.

Klebs considered that tuberculin exerted a transforming action on the tubercle tissue, restoring it to normal conditions.

Bâbes and Proca by some experimental evidence assumed a ferment activity primarily excited by tuberculin to act on the poison stored in tubercles.

The most recent explanation by Behring has some elements of similarity with that of Bâbes and Proca. Owing to the discovery of agglutination or precipitation phenomena in tuberculous blood-serums, Behring thinks that the smallest arterioles near the tubercles secrete anti-bodies of the kind mentioned (precipitins), thus causing intravascular coagulation by encountering the toxin as soon as the anti-bodies appear. This leads to the extravasations and other phenomena of the local reaction. The general reaction is less specific and due to free toxin. It is clear, from this latest explanation, why the local and general reactions gradually lessen and disappear with rapidly increased doses of tuberculin if we assume that with repeated injections of tuberculin many cells other than those immediately surrounding the tubercle acquire the power to secrete specific precipitins. The toxin injected is thus bound elsewhere and prevented from exerting a direct influence on the tubercle tissue. In favor of this explanation is the gradual return of tuberculin-reaction susceptibility after the cessation of injections and the accompanying decrease in precipitation power. It may also be possible that the local reactions promote the removal of stored toxin in tuberculous foci and thereby lessen the reaction susceptibility.

The marked fever susceptibility of tuberculous subjects is not apparently dependent upon the presence of a local reaction or congestion of tuberculous foci. It is often revealed by transient causes, such as excitement, indigestion, and by the injection of non-specific irritants—nucleins, albumoses, etc. Whether or not there is always a slight increase in toxin absorption from the foci due to more rapid blood- or lymph-flow is not known. The fever reaction is not infrequently obtained from a small dose of tuberculin without evidence of local disturbance. The reason for this susceptibility and its relation to tuberculin is not as yet fully understood.

IMMUNITY.

Against the Toxins of Tubercle Bacilli.—The repeated injection of various tuberculins or products of tubercle bacilli results in a gradually increased tolerance to the same. This habituation or immunization occurs not only in healthy but also in tuberculous animals, though less easily and uniformly in the latter, owing to the already diseased conditions. Koch early recognized the rapidly increased tolerance to tuberculin attained by tuberculous subjects, and provisionally explained it by the assumption that the tuberculous foci were being destroyed. Later developments in the field of immunity showed that the habituation was similar in many respects to that obtained with other poisons of proteid nature.

The dosage of tuberculin, like other bacterial poisons, could be gradually or rapidly increased to a point, varying in different animals, beyond which chronic poisoning was liable to develop with symptoms characteristic of the poison employed for immunization.

It was also found that by injections of tuberculin in full doses, continued for long periods, no higher degree of resistance was attained either to the toxic doses or to subsequent infection with the disease.

Moreover, there was danger even in this way of producing slow poisoning, as evidenced by loss of weight, anemia, and debility. There are, therefore, close analogies in the behavior of animals toward tuberculin injections and their reactions to the toxins of other bacteria, such as typhoid, diphtheria, anthrax, etc.

Antitoxins.—When first the discovery of antitoxins made way for a better understanding of the processes by which habituation to bacterial toxins was brought about, it was but natural to expect to find anti-tuberculins associated with the development of tolerance to large doses of tuberculosis toxins.

Maragliano was among the first to report successful results from serums thus prepared. He claimed that small reacting doses of tuberculin could be inhibited in their effect when mixed with the serum of animals immunized by tuberculin. Behring and Knorr observed the same fact with relation to human serum obtained from patients undergoing tuberculin treatment. Nieman claimed similar results with goat serum. Viquerat and Fisch claimed that they found anti-tuberculin in mule and horse serum, respectively using tuberculins of different kinds for immunization.

Boinet obtained immunizing effects with anti-tuberculin serum from goats. Redon and Chenot with ass and mule serums prolonged the course of guinea-pig tuberculosis. de Schweinitz and Dorset produced similar results with immunized cow serum, and later with horse serum.

Bâbes and Proca and Jourkine noted a lengthening of the tuberculous process in animals injected with immunized serums, but antitoxic properties were weak. Paterson with chickens, and Behring with cattle and horses inoculated with dead tubercle bacilli or their products, found antitoxic power, but the serums were too irritating for use. A like result followed the extensive experiments of Maffucci and Vestea, who found that their sheep serums produced effects like tuberculin. Trudeau and Baldwin with horse, ass, cow, fowl, and rabbit serums prepared in various ways were unable to note antitoxic effects. Auclair also failed with fowl serum.

The difficulty in proving the presence of anti-tuberculin can thus be judged to be much greater than might be expected, and the relapsing or chronic character of the disease makes any therapeutic test easily fallacious either for or against its activity. The neutralizing power of all serums thus far produced upon tuberculin is relatively weak when compared with diphtheria or tetanus antitoxin.

Agglutinins, or Precipitins.—Moreover, since a further insight into immunity problems has been obtained by the discovery of agglutinins and precipitins in connection with tuberculosis serums, it may well be questioned whether the anti-tuberculin serums contain any true antitoxin. By the recognition of agglutination properties, which cause clumping and sedimentation of tubercle bacillus emulsions in serums of tuberculous individuals, Arloing and Courmont opened a new field for research, which is unquestionably of great importance to the correct understanding of the mechanism of specific resistance against tuberculosis.

The connection between this agglutination reaction and resistance has been noted by Arloing and Courmont, who obtained positive results more frequently in the earlier stages of pulmonary tuberculosis before toxemia had developed to a serious extent.

Koch established the same fact later with patients under treatment with emulsions of pulverized tubercle bacilli. At the same time Koch demonstrated that the tissues of animals responded to the injection of these emulsions by the production of agglutinins, increasing in power in the serum until the limit of stimulation was reached, beyond which toxemia might ensue.

Precipitins.—Levene readily produced specific precipitating power in the serum for the original tuberculin by a few injections into healthy rabbits; and as the emulsions of pulverized tubercle bacilli employed by Koch, Romberg, and Köppen are really solutions of the toxin to a great extent, it is more accurate to regard the sedimentation phenomenon named "agglutination" as a true precipitation. Specific precipitins can be produced by the injection of tuberculin subcutaneously or intraperitoneally into rabbits that have not only the power *in vitro* of coagulating and precipitating a certain amount of tuberculin solution, but also of agglutinating emulsions of bacilli (Baldwin*). It is difficult to completely precipitate all the active substance from solutions of tuberculin by an excess of serum so that no tuberculin-reaction power remains in the solution. The reaction, may, however, be weaker.

The sediment is inactive as such, but when brought into solution with weak alkali produces tuberculin reactions.

Maragliano's serum has precipitation power with the homogeneous culture of Arloing and the emulsion of Koch. It is probable that other anti-tuberculous serums also contain precipitins, but whether or not their activity wholly depends upon these bodies is yet in question. The possibility of a multiplicity of anti-bodies having affinities for the tubercle bacillus or its products is to be borne in mind in this connection.

Nothing is yet known as to the source of the precipitins for tubercle bacilli, whether from special cell groups endowed with affinities for this particular bacterium or from the cells at large.

Note.—The production of precipitins for tuberculins undoubtedly is controlled by the biological laws governing other anti-bodies of like nature. The stimulating injection produces an excess of the substances known in the terminology of Ehrlich as cell receptors. At first these are largely bound to the injected toxin, but as further receptors are produced an accumulation occurs in the serum which reaches its height from nine to twelve days after the injection. If no further stimulus occurs, the specific receptors or precipitin gradually disappear from the serum. If too large or long-continued injections are given, the power of reproduction of the functionating cells is weakened or destroyed. The bearing of these principles upon tuberculin used therapeutically is obvious.

Immunity Against the Tubercle Bacillus.—Inoculations of weakened tubercle bacilli for the purpose of immunization or the treatment of tuberculosis were attempted as early as 1883. V. Bâbes, Falk, Martin, Solles, Hericourt and Richet, and others employed inoculations of cultures or injections of their products, with little result. Trudeau observed a favorable influence in tuberculosis of the eye from previous inoculations of avian tuberculosis in rabbits. Koch failed to note any immunizing effect from the original tuberculin administered before infection of the animals, but with other preparations Koch and Behring succeeded later in creating a high degree of resistance.

The best results in protecting animals against after-infection, however, have been obtained by living but modified bacilli inoculated intravenously. de Schweinitz, Trudeau, Pearson and Gilliland, Behring, and Thomassen have all succeeded in conferring marked protection by inoculations of weak and attenuated human bacilli upon various animals. Marked protection is to be seen in cattle against subsequent inoculation with bovine bacilli as the result of a single small dose of tubercle bacilli of human origin, and even guinea-pigs and rabbits recover at times after highly virulent inoculations following the vaccination, which killed controls in a short time (de Schweinitz, Trudeau).

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* Studies from Saranac Laboratory.

Mechanism of Immunity.—Since none of the products of cultures appear to confer the degree of protection obtained from living bacilli, it is possible that the weak virulent bacilli used in immunizing, being successfully overcome by the tissues, set free other poisons than those produced in cultures. This may then immunize the tissues against further attack for a greater or less length of time. The fact that intravenous inoculations seem to be the most efficacious for purposes of immunization suggests that the intravascular coagulation and agglutination phenomena have much to do with specific resistance. The marked reaction seen after inoculation of the eyes of immunized rabbits is very significant. During the first week control animals betray no evidence of a reaction to the inoculation except a transient redness due to traumatism. On the contrary, protected animals are ill from the beginning with high temperature and local reaction resembling a continuous tuberculin effect. After ten days the inflamed condition lessens, the cornea clears gradually, finally leaving a good cicatrix in most cases when the inoculation is properly graduated as to its virulence and quantity. The controls, however, now begin to show more and more evidence of disease, until the eyes are destroyed or badly invaded with caseating tubercles.

It is evident that a principle is involved in this reaction important in relation to immunity or resistance to tuberculosis. Whether it is simply the expression of precipitation action such as is produced by tuberculin, according to Behring (see Theories of the Reaction, page 69), or whether other antagonistic forces are brought into play which assist in the bacteriolysis of the tubercle bacillus, remains unknown as yet. The limitations of the protection conferred by preventive inoculations against bovine tuberculosis are shown by the report of Neufeld, and the duration of the immunity is as yet undetermined.

OCCURRENCE OF TUBERCLE BACILLI OUTSIDE OF THE BODY.

THE TUBERCLE BACILLUS AS A PARASITE.

Before we can approach the problem of how the bacilli invade the body, we must determine their source; in other words, discover where in ordinary life the possibilities of an infection are incurred.

The biological characters of the tubercle bacillus are such, as we have already seen, that it is unable to develop or to multiply *extra corpus.* For, granted that the organism were to find a suitable medium, it would still lack the equable grade of temperature necessary to its vitality, namely, 30° C. And even were this condition also provided, it would soon be deprived of its food, stifled, and destroyed by the ubiquitous and luxuriant flora of decomposition.

The tubercle bacillus is limited to the human and animal body, where it finds a suitable nutritive medium and a favorable temperature, and where also it is at least temporarily protected against overgrowth. Wherever, then, we meet with tubercle bacilli in nature, we are compelled to refer their origin to some tuberculous individual or animal.

THE HUMAN AND ANIMAL BODY AS A SOURCE OF PROPAGATION.

How and under what circumstances does the tubercle bacillus leave the human or animal body?

A number of tuberculous diseases, especially in those organs closed to the exterior, are associated with a production of tubercle bacilli so inconsiderable as to exclude them from any responsibility in the dissemination of the disease. On the other hand, a prominent rôle is played by the chronic forms of the disease, prolonged for years and accompanied by a free production of the bacilli. This is especially the case where organs are implicated which communicate with the surface and continually deliver germs to the exterior; as, for example, the respiratory tracts.

The prevalence of tuberculosis among animals, especially the domestic animals, is well known. As it is here mostly a question of more or less circumscribed foci, and as the animals are killed as soon as the disease becomes at all evident, the production of bacilli and the danger of their dissemination are limited to within rather narrow bounds. Nevertheless, it is possible for the feces, the urine, and the purulent secretions, but far more for the milk used as food, to act as a source of propagation of the disease; and there is some danger, although slight, from the meat after death.

[The relation of human to bovine tuberculosis has been the subject of much heated discussion in the past three years.

In 1868 Virchow insisted that human and bovine tuberculosis were different diseases. In 1898 Theobald Smith, after experimenting with cultures of tubercle bacilli derived from man and from cattle, stated that "we are justified, if only to guide and stimulate further study, in establishing a distinct human and bovine variety of tubercle bacilli."

Previous to this Chauveau, Bollinger, Frothingham, and others had shown points of difference between the two organisms, and had assumed their non-identity.

Koch, in 1882, with the announcement of the discovery of the tubercle bacillus, stated that bovine tuberculosis—known as "pearly disease"—and human tuberculosis were one and the same.

At the London Tuberculosis Congress in July, 1901, Koch took the opposite position, stating that, as the result of further experiments, he had concluded that the bacilli of bovine tuberculosis were not capable of producing ordinary tuberculosis in the human being, and that he did not believe that either meat or milk from tuberculous cattle was dangerous to man; also that he had found it impossible to infect calves with tubercle bacilli from men.

These conclusions were the result of extensive experiments, in which unsuccessful attempts had been made to infect animals by inoculation and by feeding with the human bacilli, as well as of careful study of the clinical relations of intestinal and other forms of tuberculosis in man.

Since the above statement was made, many investigations have been carried out with the view of establishing the exact relation of these two forms of tuberculosis to one another, but, up to the present, it must be admitted that this question in all of its relations has not been finally settled.

The weight of evidence and the weight of opinion are against the doctrine of the strict duality of tuberculosis as maintained by Koch, and confirm the view that the two forms of the disease are interchangeable.

Before the publication of Koch's statement, several observers had obtained positive results by inoculating human tuberculosis upon cattle (Crookshank,[1] Orth,[2] Bollinger,[3] Chauveau,[4] Frothingham,[5] Martin,[6] Paterson,[7] Hamilton,[8] Arloing,[9] Behring.[10] Subsequently many others (Delapine,[11] Ravenel,[12] Arloing,[13] de Jong,[14] Prettner,[15] Thomassen,[16] Wolff,[17] Hamilton and Young[39]) similarly succeeded in infecting cattle with bacilli from human sources.

These results furnish positive proof that human tuberculosis is inoculable upon cattle, but it must be noted, as a rule, the lesions thus produced, when compared with those following the inoculation of bovine tuberculosis upon similar animals, showed a relatively less extensive development, a slower growth, and a greater tendency to spontaneous cure.

Koch's second proposition that bovine tuberculosis is not pathogenic for human beings is much less susceptible of direct investigation. Many cases, however, have been reported (Pfeiffer,[18] Tscherning,[19] Coppez,[20] Hartzell,[21] Jadassohn,[22] Ravenel,[23] de Jong[24]) in which there is a fairly clear history of the direct inoculation of bovine tuberculous material, resulting in a tuberculous lesion, which, however, in most cases, was purely local in character, and but rarely showed a tendency to become generalized.

de Schweinitz and Schroeder[25] and MacFadyean[26] compared the effect of inoculations of human and bovine tuberculosis upon monkeys, hoping to throw some light upon the question by the selection of the creatures that were closest to man in the animal series. They found that monkeys are at least as susceptible to bovine as to human tuberculosis. de Schweinitz repeated experiments that had been made before, comparing the effect of tuberculin obtained from different sources, and confirmed results already obtained by others. He could discover no difference in the reactions following the injection of bovine and human tuberculin.

The above results are adequate proof that the two forms of the disease are, in some degree at least, interchangeable. But it is equally clear from them that bacilli from bovine tuberculosis are more virulent for cattle, those from human tuberculosis for man.

It has long been known that there are certain morphological and biological differences between the bacilli from the two sources; differences in form, differences in growth and relation to various media, and in their reaction to temperature (Smith,[27] de Jong,[28] Ravenel[29]).

Trudeau and many others have found tubercle bacilli susceptible of very marked change in pathogenicity by a sojourn in the bodies of various animals. Trudeau,[30] Behring,[31] and de Schweinitz,[38] moreover, have demonstrated that the bacilli after cultivation through many generations in artificial media no longer kill guinea-pigs, although they preserve most of their external features.

Behring[32] finds that the toxicity of cultures of tubercle bacilli depends upon their origin, their treatment during growth, etc., but that only one kind of tubercle toxin can be found. This identity of the toxin found in all preparations of tubercle bacilli tends, he believes, to prove the identity of human and bovine tuberculosis. He employs human bacilli for immunizing cattle.

Ravenel[33] isolated from the mesenteric glands of a child who died of primary intestinal tuberculosis a bacillus which had the most intense pathogenic power for cattle. He also succeeded in intensifying for cattle the pathogenic power of a human culture of moderate virulence by passing it successively through calves.

The marked rarity of primary intestinal tuberculosis in children in spite of the great frequency of tuberculosis in cattle upon whose milk the children are nourished, is probably to be explained upon the ground of the relatively slight pathogenicity of the bacilli for children when taken fresh from their bovine source, as well as by the normal protective mechanism of the body.

Behring[34] has recently suggested that pulmonary tuberculosis, developing later in life, is the result of an infection, acquired through the intestine at a very early age, from milk—an infection which, in the mean time, has remained latent, but later is called into activity by circumstances which diminish the vitality or resistance of the individual. This view is based largely upon his observation that, during the first few days of life in mammals, the normal, uninjured membrane of the alimentary tract permits the passage of bacteria with great readiness. These observations, however, require confirmation.

The weight of general clinical evidence, and a study of the environment of the patients, is in favor of the view that most cases of pulmonary tuberculosis, and most cases of intestinal tuberculosis in children, are the result of contact with consumptives, it being remembered that generally the intestinal form of the disease is secondary to a lesion in the lungs or bronchial lymph-glands (Holt,[35] Northrup,[36] Bovaird[37]).

In conclusion, after reviewing the evidence, the present state of our knowledge may be summarized as follows:

1. The bacilli of human and bovine tuberculosis are the same organism, but modified in their activity by change of host. By transmission through cattle they acquire increased virulence for cattle, but lessened virulence for man.

2. There is good reason to think that primary tuberculosis of

the alimentary tract in infants is acquired chiefly from milk of tuberculous cows, but it must be remembered that primary intestinal tuberculosis is a very rare condition.

3. The doctrine of the hematogenous origin of pulmonary tuberculosis, either as an immediate result of an intestinal infection, or as the outbreak of an infection latent since early infancy, has yet to be proved, but must at present be regarded as a possibility.

Finally, in view of all the facts that are at hand, we are not justified in relaxing in any measure our efforts to prevent the use of tuberculous milk and meat, or to prevent the dispersion of bacilli by the sputum of consumptives.—Ed.]

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By far the most important source of infection for human beings is the tuberculous individual himself, and especially he in whom the destructive process has localized itself in the lungs: the consumptive. The enormity of the peril from this source may be judged from the fact that one-seventh of the number of all deaths are due to phthisis, and that the majority of those so afflicted produce bacilli for weeks and months, nay, even for years, and distribute them in their environment.

The danger of propagation of the tubercle bacilli post mortem is hardly to be considered, since after burial the life-period of the organism is limited through the process of decomposition.

Bacilli in Earth-worms.—It may be recorded as a curiosity that Lortet and Despeignes kept worms for some time in earth mixed with tubercular sputum in flower-pots, and succeeded in finding tubercle bacilli in the worms themselves and in their excrement; but actual practical importance is hardly to be ascribed to this experiment.

The feces and the urine are of less significance in infection, since they are for the most part poor in bacilli, and are moist when voided. They pass into the privy, and are soon robbed of their virulence by putrefactive processes. Among animals there is, indeed, no such regular method of disposing of the ejecta; nevertheless the germs of the disease are likewise subject to early destruction through the swift process of decomposition.

The presence of tubercle bacilli in the secretions of the larger animals is, as it seems to me, underestimated. Koch goes so far as to say: "Animals produce no sputum, as is well known, so that no bacilli are thrown from their respiratory passages into the atmosphere during life." Further researches have taught that such is in fact the case with guinea-pigs and rabbits, but that the secretions of the larger animals do not so rarely contain bacilli, especially when the disease pursues a chronic course.

Even before the discovery of the tubercle bacillus, Toussaint produced tuberculosis in a rabbit by means of the nasal mucus of a diseased cow. Siegen found the tubercle bacillus in the muco-purulent exudate from the vagina in cases of uterine tuberculosis in the cow. These results demand consideration as regards at least the immediate environment of tubercular cattle, the more especially as the possibility of desiccation and dissemination in the form of dust is here not excluded.

Far more important to human beings is tuberculous milk and the flesh of tuberculous animals, in so far as it is employed without prophylactic precautions. If the udder itself be the seat of tuberculous disease, the tubercle bacilli are found almost invariably in the milk; at times, even though the udder is free, bacilli are found in the milk if there is a severe tuberculous process elsewhere in the animal. (See chapter on Intestinal Infection.)

DISSEMINATION OF TUBERCLE BACILLI THROUGH THE SPUTUM.

Ubiquity.—The chief rôle in the dissemination of tubercle bacilli undoubtedly belongs to phthisical sputum; and the enormous number of bacilli which it contains stamps it as the most redoubtable enemy of the race. It has in fact been calculated that a single individual can produce daily 7200 millions of bacilli, from which the conclusion is only too obvious that a consumptive, if he permits his sputum to dry, is capable of infecting a very wide circle. For a long time all the biological peculiarities of the tubercle bacillus were unknown. Its existence was believed to be absolutely beyond our control. All the laws of physics with regard to gravitation were ignored. Every breath of the consumptive was pictured as loaded with tubercle bacilli, which the winds carried broadcast. To this was added the notion of miasma, which at that time was entertained by many investigators; and scientists, piling error upon error, adopted the direful theory of ubiquity—direful, because it reflected upon every prophylactic procedure as necessarily futile. According to this conception, tubercle bacilli are universally distributed through the atmosphere wherever there are men, and every man must continually inhale them.

How do these exaggerations compare with the bare facts of the case?

ATTACHMENT OF GERMS TO DAMP SURFACES.

The doctrine of ubiquity was perforce somewhat limited by the fact that corpuscular elements, consequently micro-organisms, are not removed from moist surfaces by currents of air and cannot be disseminated by evaporation. In other words, sputum while moist is without danger, except in those rare cases in which it comes into actual contact with wounded surfaces. Furthermore, decomposition processes are very rapidly set up in moist sputum, and serve to destroy the tubercle bacilli; and thus it happens that the material is mostly rendered innocuous and deprived of its rôle as a carrier of infection.

THE AIR OF EXPIRATION GERM-FREE.

For the same reason, the breath of consumptives, which was so long held in suspicion, is really without danger, because the bacilli are unable to free themselves from the moist lining of mucous membrane which coats the entire respiratory tract, and so are unable to pass out with the air of expiration. Tyndall had already shown that expired air was to the eye unpolluted, and contained no solid bodies of any description. The adherence of germs to moist surfaces and the purity of the air of expiration has been further established by many researches of Nägeli, Nägeli and Buchner, Wernich, Gunning, Celli and Guarnieri, Kümmel, Fr. Müller, Sormani and Brugnatelli, Charrin and Karth, Straus and Dubreuilh, and confirmed by the experiments of Tappeiner, Sirena and Pernice, and Cadéac and Malet. In the experiments of the last-named authors animals were exposed to the breath of consumptives or to the air which had passed through phthisical sputum, without subsequently showing any traces of disease. Isolated contradictory reports from Giboux, Ransome, Karst and Bollinger are vitiated from the outset by errors of technic and hardly serve to discredit the above conclusions. It may therefore be regarded as established beyond doubt that the air of expiration is under all circumstances free from the bacilli and the spores of tuberculosis, even though it comes from cavities and has passed over tuberculous organs. Further, sputum, as long as it remains moist, is incapable of yielding bacilli to the atmosphere.

DISSEMINATION BY MEANS OF FLIES.

Spillmann and Haushalter drew attention to the fact that the germs of tuberculosis might possibly become distributed through the air and upon food by means of the house-fly. They found tubercle bacilli in the abdominal cavity and in the feces of flies which had sucked at the sputum cloths of consumptives. Hoffmann fed flies directly with tuberculous sputum, and was able similarly to identify tubercle bacilli in the fecal matter of these animals, which perished rapidly. Five inoculations undertaken in relation with this research produced one case of tuberculosis in a guinea-pig. When we consider, however, that flies are limited to a few months of the year, and that the amount of their dejecta in comparison to a single expectoration is really minimal, we shall hardly be disposed to attach much practical significance to this mode of distribution.

DRIED SPUTUM.

Dried sputum alone, therefore, is a source of considerable danger. Drying of the sputum occurs primarily upon the street and in dwellings where the patients spit upon the ground or into their handkerchiefs. This danger must be properly estimated, and in such an estimate not only the number but also the vitality and proliferative capacity of the bacilli are to be considered; and all those factors must be taken into consideration which tend sooner or later to impair the vitality of the bacilli, independently of our interference.

Dead Bacilli in Sputum.—Koch had already shown it to be extremely probable that the tubercle bacillus as an individual entity frequently has only a very brief existence in the body. Kitasato proved experimentally that the majority of tubercle bacilli in sputum or in cavities were already dead, even though indistinguishable microscopically from the living forms. From this fact we are not to deduce, as is frequently done, the absence of any danger in sputum, for it is easy to convince ourselves by inoculations that, among the thousands of bacilli which we thus introduce into the animals, some are always alive, and are capable of proliferating and of ultimately destroying the animal. Nevertheless the danger is small compared to the earlier conception of it, and the overstatement of the possibilities of infection is revealed in its full absurdity by Kitasato's discovery.

Limited Vitality of the Tubercle Bacilli.—The still virulent forms have also a very limited existence, even when the sputum has dried up. After about six months, even large quantities of expectorated material contain not a single germ capable of further development—the bacilli have died off. It is therefore illogical to speak of a place or of a dwelling as saturated with the accumulated growth of years of bacilli.

Bacilli in Nature.—This experimentally determined maximum of a half-year's existence is reached only very exceptionally by bacilli dried under ordinary conditions. It has already been shown that tubercle bacilli perish within from a few minutes to hours when exposed to direct sunlight, and within a few days when exposed to diffuse light. Sunlight is therefore a disinfectant without peer, and to this is due the fact that virulent bacilli are not found in any considerable number in the external world. Furthermore, the bacilli which are cast abroad become lost in the immeasurable expanse of atmosphere.

In addition to light and atmosphere, the cleansing of streets in well-ordered communities plays a very important rôle in disposing of the phthisical sputum which is thrown upon the pavements in great quantities in populous cities. In Berlin, for example, 848,478,000 liters of water were used in seven months for street-sprinkling; and upon fifty-two days during this period sprinkling was omitted on account of rain and sufficient moisture. To this quantity of water must be added the uncounted amounts which descend yearly in the form of mist, snow, and rain. In the present winter, which was in no wise exceptional, 225,610,000 liters were carted away. All this water keeps the bacilli from drying, and washes them down the sewers after they have been rubbed off the ground by the constant friction of passing feet and of the wheels of wagons. It is, therefore, conceivable that only a minimal proportion of virulent bacilli remains, and this is then scattered through such an enormous quantity of air that it hardly comes into play, and its inspiration becomes an extremely improbable event.

BACILLI IN THE DWELLING.

Very different is the condition of affairs when sputum is allowed to dry within the dwelling. Here the sun and the atmosphere play a far less active rôle than outdoors, where the destructive influence of light has full and undiminished play. In dark places there is the greatest danger of infection, and narrow alleys, courts, and dwellings shut off from light have always been rightly regarded as the special breeding-places of tuberculosis and scrofula. How long dust can maintain its virulence, especially in a dark room, was evidenced by one of the author's investigations, by which it was shown that dust in the neighborhood of a bed upon which a consumptive had died six weeks before still contained virulent bacilli. (See Bibliography: Cornet.)

In a room bacilli are distributed within a relatively narrow space, 30 to 50 cubic meters, in which they may under certain circumstances accumulate for days, weeks, or months. In addition, the air is often insufficiently renewed, so that even upon this ground a comparison with the conditions prevalent in the external world, even though so many consumptives cast out their sputum there, cannot fail to reveal an enormous difference in the proportional content of bacilli. The process of moist cleaning of the floors serves to a certain extent as a substitute for the meteorological conditions in nature, and diminishes the number of infectious germs in the dwelling; yet such is dependent upon the individual sense of each householder. Accordingly, the danger of infection upon the streets is evidently far less than within the house. In the former, nature espouses the otherwise hopeless cause of extermination; while in the latter the natural allies, air and light, are only too frequently excluded.

These theoretical conclusions are confirmed by practical experience.

EXPERIMENTAL DEMONSTRATION OF THE BACILLI IN DUST.

Very soon after the discovery of the tubercle bacillus scientists attempted to demonstrate its presence in various situations outside of the body; but, in notable contrast to the general theory of its ubiquitous distribution, it was nowhere to be found. The researches along this line of Williams, Celli and Guarnieri, von Wehde (under Bollinger's direction), and Baumgarten remained barren. The author, likewise, only succeeded in revealing their presence through the fact that he sought them in places where infections are by experience found likely to occur—namely, in the immediate environment of the consumptive. The author selected the natural sediment of the air, the dust deposited from it, in the justifiable assumption that the tubercle bacilli in the atmosphere could maintain themselves as floating particles only for a brief period of time; and that, following the laws of gravity, they would settle in the same manner as dust; it being a known fact that even in heavy media such as pus they tend to seek the bottom. In the investigation the author made use of the dust from places in which a direct* pollution by tuberculous sputum (either such as had been expectorated, or coughed up, or deposited by dirty fingers, cloths, cups, or otherwise) was almost incredible.

The question of the vitality of the tubercle bacilli was not to be settled by microscopic investigation, but only by animal experimentation. The latter method, especially the intraperitoneal inoculation of guinea-pigs, affords by general consent so delicate a test for the presence of tubercle bacilli that not even a very minute proportion of them in the dust could escape detection, but would necessarily give origin to a more or less outspoken peritoneal tuberculosis. The result of the investigation is briefly indicated in the Table on page 86.

It appears, therefore, that as a rule tubercle bacilli occur in virulent condition only in dwellings, institutions, factories, and hotels, in proportion as these are occupied by consumptives. Tubercle bacilli were found in the immediate environment of consumptives only when they were careless with their sputum, voiding it upon the floor or into their handkerchiefs and thereby giving it occasion for drying and dissemination by dust. But even under such circumstances, the infective area was relatively narrow because the markedly hygroscopic quality of the dried, sticky, mucin-rich sputum and of the mucin-rich bacilli opposed to a certain extent fine subdivision and wide dissemination, especially when the air was not in active motion.

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* As far as the author is aware, Baumgarten alone raised the objection to these researches that possibly the walls from which the dust was taken were contaminated by the ejecta of flies which had fed upon contents of sputum-cloths of consumptives. This objecton is, however, best refuted by the fact that just where spit-cloths were used, affording the flies an opportunity to feed, bacilli were absent, and where handkerchiefs were used, denying them that opportunity, bacilli were found. Moreover, these flies had long been away. If Volland believes that the bacilli on the wall came not from the air, but from the shaking-out of bed-linen (through the air, notwithstanding?!—Author), he is confuted by the fact that they were found in places where there were no beds; *e. g.*, factories.

	Number of Tests in All.	Number of Tests in which at Least One Animal was Tuberculous.	Number of Cases in which the Animals Remained Healthy.	Number of Animals Employed.	Number of Animals Dying of Disease Other than Tuberculosis.	Number of Animals which became Tuberculous.	Number of Animals which Remained Healthy.
In 7 hospitals ..	38	15	12	94	52	20	22
In 3 asylums ..	11	3	6	33	16	13	14
In 2 prisons ...	5	—	4	14	6	—	8
In an inhalation room ...	2	1	1	4	—	2	2
In dwellings and work places of private patients:							
(a) with positive result ..	27	21	—	75	38	34	3
(b) with negative result ..	35	—	22	95	53	—	42
Polyclinic, orphan asylum, pathological institute	12	—	9	28	14	—	14
Surgical ward ..	3	—	3	8	1	—	7
Streets, etc. ...	14	—	12	41	16	—	25
Total	147	40	69	392	196	69	137

Further investigations by Rembold, Schliephake, Krüger, Kastner, Bollinger, Kustermann, Enderlen, Prausnitz, Petri, and Martin Kirchner confirmed the author's results in both their positive and negative aspects. Kirchner, for instance, noticed that in the fall of 1893 an orderly, in June of 1894 a sergeant, and in May of 1895 another sergeant, all of whom had previously done duty for some length of time in the uniform room, died of pulmonary tuberculosis; in the dust of the uniform room he was able to demonstrate virulent tubercle bacilli by inoculation experiments.

In all, 400 dust tests have up to this time been made upon more than 700 animals; enough to justify certain general conclusions.

The author assumes that in such places as did not reveal the presence of bacilli none were actually present, because, in the first place, the dust was taken from the immediate vicinity of the consumptive, where there was the greatest chance of finding the tubercle bacilli in case they had passed into the air; second, the quantity of dust investigated was sufficient, since it represented a precipitate of at least 51,000 liters of air, more than a man inspires in 102,000 respirations; third, the intraperitoneal inoculation of guinea-pigs affords an absolutely sure test. It has indeed been calculated that 43 (?!) tubercle bacilli in sputum, of which, moreover, the majority are dead, will with absolute certainty produce a tuberculosis. These results yield a picture which corresponds to the actual distribution of tubercle bacilli outside of the body.

On theoretical and practical grounds, the belief in the ubiquity of the tubercle bacilli may be considered absolutely discredited. The tubercle bacillus is found, as a rule, only in places in which an uncleanly consumptive maintains himself; otherwise it occurs but rarely.

In the open, in the dust of streets, it has hitherto been impossible, in spite of numerous trials, to find tubercle bacilli in places protected from direct expectoration. Upon the ground itself they may frequently occur, but all the above-mentioned factors unite in accomplishing their destruction and prevent their pulverization, so that the danger of infection in the open plays no very alarming rôle.*

This assumption is confirmed, as I showed at the time, by the fact that street sweepers who breathe this dust continually very rarely are affected with tuberculosis, even though they follow their arduous occupation for years (some even thirty to thirty-five years); and subsequent investigations of the author gave the same result for coachmen.

Schnirer's investigation, which revealed the presence of tubercle bacilli in the washings from grapes which were exposed for sale upon the streets in Vienna, admits of the possibility of contamination by means of infected street dust or through the tuberculous sellers or buyers, assuming that this isolated research was really carried on with full bacteriological precautions.

CONCLUSIONS.

The result is as follows: On the part of tuberculous animals dissemination of tubercle bacilli by means of urine and feces is practically ruled out by the rapid process of putrefaction. Somewhat more importance, at least for certain cases, attaches to the infectious nasal mucus and even more to the infected flesh and milk, which may convey the disease in the shape of food. On the part of tuberculous human beings, feces, urine, and pus play relatively small rôles, partly on account of their insignificant content of bacilli, partly on account of early putrefaction. The greatest importance belongs to the sputum, not, however, when moist, but when dried up and given the opportunity of dispersion.

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* It is occasionally stated that Marpmann found tubercle bacilli in the dust of streets. A bacteriologist will hardly accept these investigations seriously, as the same author also succeeded in producing pure cultures from sterilized (?!) tubercle bacilli.

CHAPTER III.

HISTOLOGY OF THE TUBERCLE.

The tubercle bacillus produces changes within the organism which, as has already been shown in the case of the dead bacilli, may be differentiated into such as are local and such as are general in character. The latter, when they have developed sufficiently, evince themselves in the form of emaciation, fever, and loss of tissue. The former, with which we are at present chiefly occupied, are very complex in character. These local changes depend for their production upon two sets of agencies: first, the influence exerted by the tubercle bacillus as a *corpus alienum,* simply through the exercise of its vital functions and of its proliferative capacity; and, second, the influence exerted by its metabolic products and its proteins.

In general terms, it may be accepted as a law that the bacilli as such, in a living condition, produce changes analogous to other foreign bodies, namely, inflammation predominantly of a productive type, whereas the metabolic products and the proteins are responsible rather for exudative processes. Practically it is impossible to make so sharp a distinction between the individual factors concerned, inasmuch as the living bacilli never come into action alone, but always in combination with the products of their own metabolism and with the proteins of dead individual bacilli. According as the one or the other of these components has the preponderance, a variety of tissue changes are found to occur; and herein, at least in part, lies the explanation of the diverse observations of various authors.

Koch had already given a generalized description of the relations existing between the tubercle bacilli and the surrounding tissues. Baumgarten made use of inoculations into the anterior chamber of the eye, and was able to follow with exactness the progressive histological genesis of the tubercle, by enucleating the bulbs at definite intervals of time. To this comprehensive and important research we are especially indebted for our more detailed knowledge of the development of the tubercle. The conditions were found to be as follows: During the first days after inoculation no change is at first noticeable, save only that the bacilli multiply rapidly and invade the surrounding tissue of the iris and the cornea both singly and in swarms; the histological structure being still unaltered as late as the sixth day. Then freshly formed epithelioid cells begin to make their appearance in places where the bacilli are more densely grouped, and this is the first stage of true tubercle formation. The bacilli increase rapidly in number and become grouped into small, dense masses, in which the bacilli themselves assume a parallel arrangement; and, corresponding to these masses, the foci of epithelioid cells are also found to increase. Within these foci one is able, by employing a suitable technic, to demonstrate single cells in a condition of indirect cellular division, of karyokinesis. From about the seventh day karyokinetic figures become very much more frequent, and the proliferative processes thus indicated involve, in continually increasing ratio, not only the fixed tissue cells surrounded by bacteria but also the actual connective-tissue cells, the endothelial elements of the vessel walls, and the epithelial cell structures. Thus, by the constant repetition of cell division, large masses of epithelioid cells, rich in protoplasm, are formed; the bacilli lying between the cells, occasionally within them, and with relative frequency one, two, or more, are found within the cells undergoing mitosis.

At this stage of free karyomitosis we find certain small round cells, poor in protoplasm ("naked"), with deeply staining nuclei, which are sharply distinguished from the large epithelioid cells, with their large, oval, vesicular, palely-staining nucleus. These are the so-called migratory cells, white blood-cells which have wandered out of the blood-vessels. They are at first rather isolated in the nests of epithelioid cells, whereas at the site of inoculation they are found in larger numbers.

As Baumgarten found the bacilli in the early stages either lying free in the tissue spaces or enclosed by the fixed tissue cells, while the migratory cells were rather infrequent at the beginning of tubercle formation, he ascribed to the latter only a subordinate rôle in the dissemination of tubercle bacilli; and he believed that their spread was due, in addition to the mere growth of the colonies, to the currents of the lymph-stream. Koch, on the other hand, had assumed that these migratory cells take up the bacilli which invade the tissues and carry them a certain distance until overcome by their perilous burden. This conception is furthered by the investigations of Yersin upon chicken tuberculosis, and is shared by Dobroklonski, Stschastny, Nelsen, and Kockel.

The same process repeats itself in the most diverse situations in the body when invaded by tubercle bacilli. They proliferate, form colonies, and give rise to the multiplication of epithelioid cells by means of karyokinetic division, as already described.

After a certain time cell division comes to a standstill. The volume of single epithelioid cells, however, increases considerably, and in some there are as many as two or three nuclei. Occasionally, also, depending upon the nature of the inoculation material, actual giant cells of Langerhans are found, which often contain a large number of oval, vesicular nuclei.

Tubercle bacilli are frequently found in these giant cells. In chronic processes, *e. g.*, scrofula and fungous synovitis, where the number of bacilli is small and where the giant cells constitute at times their exclusive domicile, this occurrence involves only isolated bacilli. But in very active processes the number of bacilli contained by a single giant cell may amount to fifty or more, and frequently the number of the giant cells stands in inverse proportion to the number of the bacilli, or, which amounts to the same thing, to the acuteness of the process.

The situation of the bacilli is noteworthy. If the nuclei of the giant cell form a closed circle, the bacilli, as a rule, occupy its center. If, however, the nuclei are clustered at one pole, the bacilli generally gather at the opposite extremity of the cells, so that one may conceive of a "species of antagonism between the nuclei of the giant cells and the parasites enclosed by the cell body" (Koch). The same conditions were found by Baumgarten and Marchand to exist in cases in which non-specific foreign bodies were completely engulfed by the protoplasm of giant cells. When, on the other hand, the foreign body only borders upon the giant cell, the distribution of nuclei is found to be irregular. Through the growth of the preëxisting cells and the formation of large numbers of new cells, the fibrillar stroma of the original tissue is continually driven further and further apart, partially split up and destroyed, so that the cells come to be separated from one another only by sparse fibrillæ. These fibrillæ by their net-like arrangement constitute the "reticulum" of the tubercle, which was first described in detail by E. Wagner. Other authors consider this network to be nothing more than a coagulation product due to the fixing agents. The centrifugal pressure due to the multiplication of cells results in a rather denser aggregation of those lying peripherally and, consequently, in a more or less well-defined delimitation of the tubercle from its environment. At the same time, the peripheral tubercle cells undergo a process of flattening out, and become arranged in such fashion that the long axes of their nuclei surround the central mass in concentric fashion. The essential factor in this encapsulation is sought by Baumgarten in the laws of growth peculiar to the tubercle, which regularly preclude any enlargement of the single focus beyond a certain point. In this stage the so-called epithelioid cells described by Langerhans, Wagner, and Schüppel are found.

With the decrease in cellular proliferation, leucocytic elements occur in continually increasing ratio; and by the tenth or eleventh day the inflammatory change in the process becomes manifested even macroscopically by the dilatation of the blood-vessels situated within the area of disease. In the distended venous and capillary vessels the white corpuscles are often discovered next to the walls of the vessels, or even in process of diapedesis. The close correspondence between these cells and those situated in the proximity of the vessels, and also those in the periphery of the epithelioid tubercles, permits of no doubt as to the origin of the latter.

The epithelioid tubercle becomes more and more densely permeated by the leucocytes, the number of which constantly increases. The large-celled structure of the tubercle is still recognized, but it gradually assumes the character of the small-celled, lymphoid tubercle (Virchow's original type of all tubercles).

In case the tissue is irritated by any injurious influence, such as a traumatism, this lymphatic infiltration may occur so early, according to Baumgarten, that the tubercle from the outset possesses the character of the small-celled type.

The bacillus has now reached the acme of its development, and forms a small, gray, translucent, cellular nonvascular nodule, ranging in size up to that of a millet-seed, and containing a larger or smaller number of bacilli. At this point caseation begins in the center, with the gradual death and destruction of the tubercle cells. The leucocytic elements are the first to show retrogressive changes; their nuclei shrink and break up, the protoplasm vanishes, the nuclear detritus loses its staining reaction; finally the epithelial cells also shrink and lose their nuclei; hyaline areas are formed (the coagulation-necrosis of Weigert), and finally a fairly homogeneous mass, with more or less numerous fatty granules, results. Macroscopically the tubercle assumes an opaque, yellowish-white appearance. The tubercle bacilli are still to be found, at first in groups, later lying free and isolated. Especially in cases of rapid cellular dissolution they retain their staining affinities for a considerable length of time, but eventually lose them, and become fragmented in the same manner as the cells. The virulence of the caseous areas, however, persists for some time after this process of destruction has run its course.

The further progress of involution is marked by a softening of the solid caseous masses. The material becomes "smeary," finally fluid, and is metamorphosed into a rather thick pus.

For a long time it was customary to regard the pus-formation as the work of certain specific germs, particularly the staphylococci and streptococci (Ogston, Rosenbach, Garré, Fehleisen, etc.). Further investigations by de Bary, von Grawitz, Kreibohm, Janowsky, and others, seem to indicate the possibility of an aseptic suppuration. Garré showed that tubercle bacilli were capable of producing pus in the osseous system without the aid of the so-called pus cocci, an observation which was confirmed by Hoffa, Steinhaus, and Krause. Koch, indeed, describes the injection of dead tubercle bacilli as a simple measure for inducing suppuration. Nevertheless, in consonance with the observation of de Ruyter and Roth that suppurative tuberculosis is associated with other micro-organisms (staphylococci), we shall do well to keep the possibility of a mixed infection continually in mind.

According to Kostenitsch and Wolkow, the development of the tubercle may be described in five phases: (1) Reactive serofibrinous exudation. (2) Aggregation of polynuclear leucocytes (owing to traumatism), which persists for a few days. (3) Reaction of the fixed tissue-cells and formation of epithelioid cells; increase of cell protoplasm; nuclear division; fixed tissue cells, as well as vascular endothelium and epithelial cells, become changed to epithelioid cells and take up tubercle bacilli; the reticulum becomes recognizable. (4) Mononuclear leucocytosis; mononuclear leucocytes, heretofore infrequent, occur in large numbers in the periphery of the tuberculous foci and in the neighboring vessel sheaths. (5) Degeneration of the tubercle, and beginning of a second polynuclear leucocytosis.

The histological evolution which has been described for the tubercle in the anterior chamber of the eye is typical of tubercle formation throughout. It occurs, in its essential features, in the various organs of the body, with this difference, that various types of fixed cells, according to the anatomical structure of the tissue involved, furnish the material for the epithelioid and giant cells. Thus, in addition to the capillary endothelium, in the lymph-glands it is especially the reticular cells, in the lungs the alveolar epithelium and the fixed cells of the interstitial connective tissue, which are involved in this metamorphosis.

As regards the share taken by the various tissue elements in the formation of the tubercle, as well as of the giant and epithelioid cells, there is still a great diversity of opinion. Virchow, in his "Cellular Pathology," considers the connective tissue responsible for the formation of the tubercle. Baumgarten holds that fixed cells, both of the interstitial and epithelial types, become converted into epithelioid cells. Ziegler and his pupils, also Hänsel, Koch, Cornil and Yersin, derive the tubercle cells exclusively or in part from wandering cells. Metschnikoff also derives the development of epithelioid and giant cells from epithelial cells, and traces them back to mononuclear leucocytes.

GIANT CELLS.

The giant cell is formed, according to Baumgarten, from a single cell of the fixed type by means of multiple division of its nucleus. Metschnikoff and Borrel, on the other hand, ascribe its origin to a fusion of epithelioid cells, following the idea previously expressed by Arnold. Kostenitsch and Wolkow believe that a serous exudate is thrown out around the bacilli, which fuses with a number of the neighboring fixed and epithelial cells; the formative stimulus of the tubercle bacilli inducing proliferative activity in their nuclei, while the coherence of the serous mass prevents complete cell division.

Kockel has paid great attention to the histogenesis of the tubercle, and does not attribute any single mode of origin to the giant cells, but inclines to believe that in the liver at least they start from hyaline capillary thrombi and endothelial cells.

The significance of the giant cells is also an unending source of dispute. Weigert interprets the giant cells of Langerhans as a partial caseous degeneration of cells in process of proliferation, in such fashion that the center of the cell, which is generally free both of nuclei and of bacilli, corresponds to the dead portions; while the margin of the cell, which is richly endowed with these structures, is homologized with the surviving portions of the dividing cells. Baumgarten sees in the giant cells an evidence of anomalous cell division, resulting from an inefficient stimulus. Metschnikoff and his pupils consider the epithelioid cells, and especially the giant cells, as defensive organs of the body, which functionate as true phagocytes and actively ingest the live and virulent tubercle bacilli, destroy them, and change them to an amber-like yellow mass. This theory of phagocytosis, tempting as it at first appears and brilliantly as it has been defended by Metschnikoff, has, as is well known, lost ground considerably within the course of the last few years.

VARIATIONS FROM THE TYPICAL MODE OF DEVELOPMENT.

Variations from the typical mode of evolution also occur, involving especially the rate of development. Cellular proliferation and migration of leucocytes proceeds rapidly in some cases, in others more slowly; the individual phases of development follow one upon another, in the same way, more rapidly, or more slowly, than normal, as the case may be. Such variations may preëminently depend upon the agents of the disease, upon their number and their vital activity. Of marked importance is the number of bacilli, whether many or only isolated organisms occupy the area of disease, whether they are all still active or all dead, or whether there is a mixture of both. The stage of epithelioid cell formation may be practically excluded as a consequence of a premature leucocytic infiltration of the tubercle. This type, which is found especially in the acute miliary tuberculosis of men, is generally associated with very energetic proliferation of the bacilli, and is considered especially malignant, inasmuch as it denotes early disorganization. On the other hand, it is customary to regard the large-celled tubercles, those with epithelioid and giant cells, which are attended by sluggish proliferation of the bacilli, as benign. Such forms are met with especially in the lymph-glands and in fungoid arthritis.

The researches of Baumgarten, Nauwerck, and others demonstrate that this experimentally determined conception of the histogenesis of the tubercle in animals is also identical with that which takes place in human tuberculosis.

CHAPTER IV.

MODES OF INVASION OF THE TUBERCLE BACILLUS.

Although it is true that the histological findings in tuberculosis of the various organs are essentially uniform, the entire pathological picture, nevertheless, is subject to many and marked variations. In one set of cells all the organs of the body are involved; in another, only those of the abdomen or of the thorax; in still another, only the glands of a certain somatic area; and in others the skin alone is diseased. This circumstance separates tuberculosis primarily from those other infectious diseases in which only certain definite organs or systems of organs are subject to attack, as, for example, the gut in cholera, the gut preëminently, too, in typhoid, but also the spleen and the mesenteric lymph-glands.

ANIMAL EXPERIMENTATION.

The cause of this variability in the conditions was for a long time undiscovered. As long as tuberculosis was regarded simply as a constitutional dyscrasia, the assumption of an unequal predisposition on the part of the various organs was a necessary corollary. A more satisfactory explanation was first afforded by the numerous experiments upon animals, and by the determination of the various portals by which the bacilli are able to gain entry into the body.

HISTORICAL DEVELOPMENT OF ANIMAL EXPERIMENTATION.

In the first period of experimental research the majority of workers followed in the steps of Villemin and limited themselves almost exclusively to subcutaneous inoculations; as Hérard and Cornil, Genondet, Roustan, Verga, Biffi, Mantegazza, Marcet, Colin, Petroff, Clark, Klebs, and others.

It was in opposition to the theory that the tubercles so produced were only a consequence of the subcutaneous cheesy foci and the latter necessary forerunners, that intravascular, and especially intravenous, injections came into use. Since the cardinal question at that time was whether tuberculosis was actually an infectious disease, it sufficed to determine the development of nodules. The attempt to establish the identity of pulmonary tuberculosis with general miliary tuberculosis was satisfied with the demonstration of such nodules in the lung. In general, the lung was considered to be more predisposed to the disease than the other organs of the body. Tubercles were occasionally observed in other places, but the somewhat obscure lymph-nodes were apt to be overlooked, the more so as the dissemination of the tuberculous virus through the body was laid to the door of the blood vascular channels.

At the same time Cohnheim's (and Salomonsen's) brilliant discovery that the anterior chamber of the eye might be employed as a site of infection developed a horde of imitators, *e. g.*, Haensell, Baumgarten, Schuchardt, Damsch, Deutschmann, Koch, Cornil and Leloir, and many more. Inoculations into the cornea, which had previously been considered immune, were successfully carried out by Haensell, Panas, Vassaux, and Valude. The conjunctiva was a frequent subject of injection experiments (Langhans, Haensell, Falchi, Valude), which resulted in local tubercle formation, especially in cases in which the conjunctiva had been previously subjected to traumatism. Depositing the virus in the injured conjunctival sac and direct injections into the tissue of the lachrymal glands had previously given negative results (Valude), except that in the latter case tuberculous foci occasionally made their appearance in the periglandular tissue.

The question of the danger attaching to the use of the flesh and the milk of tuberculous animals could be solved only by feeding experiments. Even previous to Koch's discovery, this form of investigation had aroused a great deal of interest; I need only mention the elaborate researches of Chauveau, Klebs, Aufrecht, Gerlach, Günther and Harms, Bollinger, Viseur, Schreiber, and Orth. Johne was able to collect records of 259 animals fed with uncooked tubercular material, excluding all cases in which the data were not sufficiently accurate; of these, 47.7 per cent. gave a positive result. Since Koch's time similar experiments have been carried out with positive results by Albrecht, Imlach, Baumgarten, Fischer, Frank, Biedert (collection of 548 feeding experiments, of which 21.5 per cent. were positive), and especially by Wesener, whose work is preëminent for its thoroughness and importance. Almost innumerable intraperitoneal injections of the most diverse tubercular masses have been carried out upon guinea-pigs and rabbits. Similar experiments have seen carried out upon larger animals (calves) by Klebs, Kitt, and others.

The invasion of the lung by dust-like material coming through the respiratory channels had already been demonstrated by the iron-filings experiments of Zenker, as also by the observations of Kussmaul and Schmidt and of Seltmann; their conclusions had been confirmed by the beautiful experiments of Knauff, von Ins, Ruppert, and especially Arnold.

The frequent occurrence of an isolated pulmonary tuberculosis very naturally suggested the idea that in this case, also, the virus was carried into the organism through the respiratory tract. Villemin, with his usual far-sightedness, had long before given expression to this theory.

It was Tappeiner's contribution to show conclusive evidence for the existence of this mode of infection, which is of such great practical importance. His method was to infect dogs by subjecting them to the inhalation of pulverized tubercular sputum, a method which was also employed by Bertheau, Veraguth, Weichselbaum and Frerichs.* Koch, the author, Gebhardt, Preyss, and others, substituted in place of the sputum pure cultures of the germ. In general, inhalation experiments met with no especial favor at the hands of investigators, perhaps because of the complexity of the technic, perhaps not least because of the danger attached, to which, notably, Tappeiner's assistant fell a victim. The direct injection of tuberculous fluids into the lungs or into the previously opened trachea was therefore generally preferred. Such experiments were made by von Lippl, Reinstadler, Küssner, Schäffer, and others.

The inhalation of dried, pulverized sputa or cultures had, as a rule, given negative results, according to the publications of Santi Sirena and Pernice, de Toma, Celli and Guarnieri, and Cadéac and Malet. As I shall detail more fully below, I succeeded years ago, and recently,† too, almost without exception, in producing pulmonary tuberculosis by the inhalation of dried material, and, at the same time, I have been able to expose the causes of previous failures in this regard. These results destroyed the very foundation of Baumgarten's skepticism concerning the frequency of inhalation-tuberculosis.

Cornil and Dobroklonski made trial of the viability of the mucous membranes to the tuberculous poison by injecting pure cultures into the vagina.

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* I pass over the attempts of Schottelius and Wargunin to demonstrate that the inhalation of non-tuberculous material also resulted in the formation of miliary tubercles, since such an error hardly needs refutation at this date.

† Hitherto not fully published.

PATHOLOGICAL CONDITIONS ACCOMPANYING VARIOUS MODES OF INFECTION.

The conditions which are found among animals furnish us with very important clues for the understanding of human tuberculosis in all its aspects, but especially of the modes of infection. There is the greater indication for a brief sketch of the findings which accompany the various species of infection, inasmuch as erroneous ideas are still widely prevalent in this regard. The majority of authors who employed the one or the other method of inoculation have unfortunately neglected to furnish accurate data upon the relative changes in the various organs, and especially in the lymph-nodes, the most important stations of the tubercle bacilli in the course of their dissemination. On this account the author bases the following statistics upon his own experiments (which number more than 3000), undertaken for various purposes. Elaborate autopsy notes were taken in about 1200 of the cases; later, however, as the conditions were found to repeat themselves, short notes were taken.

In order to study the evolution and the gradual distribution of the disease, such of the animals as did not naturally succumb were killed at definite intervals of time after the inoculation. For the most part guinea-pigs were employed, rarely rabbits. The infection was produced, as a rule, by the use of tuberculous sputum or pure cultures. I would characterize the difference between the two species of animals by saying that in rabbits the tissue opposes a somewhat more sturdy resistance to the advance of the process, especially to its dissemination along the lymphatic channels, whereby the possibility of a complete arrest is also favored.

The results of inoculation may be grouped in the following fashion:

Subcutaneous Infection.—In subcutaneous injections at one side of the hypogastric area (autopsies on over 240 animals) the site of injection was rapidly involved in plastic inflammation. After a few days it generally broke open and gave way to a cheesy, purulent, ulcerative focus. During the first two or three weeks, as a rule, only the inguinal gland upon the same side was inflamed; later also that of the opposite side, with subsequent caseation and softening. The peritoneum was ordinarily normal, or but slightly injected. The spleen was involved in the tuberculous process from about the thirtieth to the fortieth day, the liver from the fortieth day. In the lungs and bronchial glands it was possible to find isolated tubercles from the fortieth to the fiftieth day; later on they became more numerous.

In animals inoculated between the toes of the hind foot (9), a slight scar appeared on the site of injection; after two weeks there was a swollen gland in the corresponding knee, and after three to four weeks, swelling of the inguinal gland upon the same side. After about the seventh week there were miliary tubercles in the spleen and the liver, while the lung was at this time still intact. Injections between the toes of an anterior extremity (6) were followed within three weeks by caseation of the cubital glands, later on of the axillary, and finally of the bronchial lymph-glands. Eventually the lungs were permeated by small nodules; the abdominal viscera were affected only in animals killed after a greater length of time.

When the tip of the ear was inoculated (4), within two months a chain of cheesy and softened glands was found to extend from the site of injection in the ear to the thoracic viscera. The lung was very markedly tuberculous, the abdominal viscera only slightly so. A similar result was obtained by injections into the internal ear (2 animals).

Cutaneous Infection.—Inunctions of the skin of the cheeks, nose, etc., with sputum (18 autopsies) were followed by a set of local changes varying in intensity with the degree of injury which the part had previously sustained. In some cases there was ulceration; in others lupoid disease; in many others only an insignificant desquamation. There was regularly, however, swelling and caseation of the cervical and bronchial lymph-glands, first of the same, then of the opposite side, followed by tubercle formation in the lungs, and eventually also in the spleen and the liver.

The fact that certain authors, especially the French, obtained negative results with their inunction experiments, leads one to suspect that they may perhaps have been unconsciously making use of the then widely distributed cultures of avian disease.

Infection of the Buccal Mucosa.—Seven animals were inoculated in the lateral pockets of the mouth, with both sharp and blunt instruments. Ordinarily after about three weeks an ulcer formed, although occasionally even after eight weeks no local change was discovered. In all cases, however, the submental, sublingual, and cervical glands, especially those of the side inoculated, became cheesy. Nodules were found in the lungs in a certain number of cases, and later on also in the spleen. The results were the same after inoculation of the tonsils (2), of the posterior pharynx (2), and of the tongue (6).

Infection of the Gut.—In the very numerous feeding experiments which were made the tubercle bacilli found their way through a perfectly normal mucous membrane into the wall of the gut (Wesener, Baumgarten, Fischer, Dobroklonski). Here they may go on to further development and form tubercles in the lymph-follicles, especially in the ileum, cecum, and colon; or, when the ingestion of large quantities has taken place, they may give rise to ulcers, which are very similar to those found in the entero-phthisis of man (Fischer); or, finally, they may find their way to the mesenteric glands, where they develop without further interference with the gut itself. With the progression of the disease, tubercles are found in the liver, whereas the lung remains unaltered or is only attacked later on.

Infection of the Respiratory Tract.—When tubercle bacilli are gently rubbed into the nasal mucosa no change occurs (12 autopsies) if care is taken not to injure the mucosa; in other cases, inflammation, reddening, and ulceration shortly make their appearance. A few weeks later the cervical glands of the same side become infiltrated and caseate, like those of the opposite side. After two to three weeks more the bronchial glands, the lungs, and finally the spleen and the liver all fall a prey to the infection.

When the animals were subjected to the inhalation of finely powdered sputum or pure cultures (over 600), within two to three weeks the lungs showed very fine, grayish-white spots, and the bronchial glands simultaneously became enlarged, with medullary infiltration. The nodules in the lungs enlarged, and, if the animals lived long enough, small cavities were formed; the bronchial glands underwent caseation. From the third to the fourth week the spleen, and later the liver, gave evidence of a beginning tuberculosis, while the peritoneum and the omentum were usually unaffected; the cervical glands were occasionally involved, though usually only in the later course of the disease. Intratracheal injections gave rise to large, cheesy foci in the lung, similar to those of a caseous pneumonia. The further course of the cases was as in the inhalation experiments.

The first attempts to produce an infection by means of the inhalation of dried pulverized sputum were made by Sirena and Pernice, de Toma, Celli and Guarnieri, and Cadéac and Malet. On the whole, they were without result, so that Baumgarten at first, and more recently Flügge, have absolutely denied the possibility of a dry inhalation. The author's earliest experiments along these lines, which were made in 1888, imbued him with the idea that these results were simply due to a technic which was faulty in that it departed from the natural conditions governing infection by means of inhalation.

Previously, the animals had been placed in closed cages, in the air of which dried, pulverized sputum was made to circulate by mechanical means. Sputum, however, as has already been pointed out, is markedly hygroscopic, and therefore immediately appropriates the moisture of the respiratory tract. It then collects into small masses, which, by virtue of their weight, can no longer be borne up by the respiratory currents, and cannot, at all events, be carried all the way to the recesses of the lung. In a fresh series of experiments in January, 1898, the author imitated as far as possible the natural conditions occurring in the dwellings of unclean consumptives. In a large room of about 76 cubic meters he distributed dried tuberculous sputum upon a carpet, and placed a number of guinea-pigs at various distances and heights from the carpet. Concerning the details the author must refer to his demonstration in the Berlin Medical Society (March, 1898). The result was that of the forty-eight animals which were thus exposed to the natural means of inhalation tuberculosis, forty-seven showed the development of tubercles in the bronchial glands and the lungs, with partial cavity formation. It follows, therefore, that dried sputum in the form of dust carries with it a very serious danger even for the extremely narrow respiratory passages of these small animals, and that it is by no means subordinate in importance to the distribution of moist, pulverized sputum. This experiment furnishes a proof of the fact, Flügge to the contrary notwithstanding, that sputum cast upon the floor and allowed to dry is divided into sufficiently minute particles for inspiration.

Infection of the Genitals.—If sputum or pure cultures were rubbed into the penis (2 cases), a widespread ulcerative process developed over the corresponding area, if a slight degree of injury, as with a fine file, were previously done to the part. If the preceding traumatism were omitted, the penis often gave no visible evidence of local disturbance. After about two or three weeks unilateral, followed by bilateral, swelling and caseation of the inguinal, then of the retroperitoneal glands, occurred. In two or three weeks more the spleen and the liver became diseased, and generally in the course of a couple of months the lungs also showed tubercle-formation. Similar results attended intraurethral injections (3 animals).

Baumgarten succeeded in producing a diffuse tuberculosis of the urethra, followed by a general spread of the disease, by injecting tubercle bacilli into the uninjured urethra of male rabbits after they had been deprived for several days preceding of food and drink.

Inunction of the vagina with sputum or pure cultures (13 cases) produced in some cases a pronounced milky secretion, in others typical tubercle-formation in vagina and uterus, and, in one case, also in the bladder; in several cases the vagina showed no change. All the animals in a short time showed swelling and caseation of the inguinal glands, caseation of the vertebral lymph-glands, and finally tuberculosis of the spleen and liver. The same results followed the injection of pure cultures into the vagina (3 cases).

Infection Proceeding from the Eye.—When tubercle bacilli were brought into the conjunctival sac (24 autopsies), subsequently subjected to a slight degree of traumatism, small ulcers formed in about two to four weeks; in other cases injection and thickening of the conjunctiva occurred. Later, there was caseation of the corresponding, then of the opposite cervical glands, then of the bronchial glands, followed by tuberculosis of the lungs and finally of the abdominal viscera. If injury to the conjunctiva were carefully avoided, it remained unchanged, and the corresponding glands became the first seats of the tuberculous advance. In one case infection did not occur.

In corneal infections (6 cases) the ulcers invaded the sclera; otherwise the course resembled that above described. When the anterior chamber of the eye was selected as the site for infection (6 cases) the author was able to confirm in all essential particulars the results of the experiments of Cohnheim, Baumgarten, and Koch. After about one or two weeks tubercles began to appear on the iris, then followed swelling of the cervical glands and of the bronchial glands, eventually tubercle formation in the lungs and finally also in the abdominal viscera.

Intravascular Infection.—The swiftest form of infection is induced by intravenous injection; for instance, into the vena jugularis or into the veins of the ear. Corresponding to the general distribution of the infectious material throughout the circulation, tubercles of practically equal maturity were found in the organs of the thorax and of the abdomen, in the lung, the spleen, and the liver. In the lungs the number of tubercles was often the greatest, because this organ constitutes the first filter in cases of intravenous injection.

Intraperitoneal Injections.—When tuberculous material is injected into the peritoneal cavity, swelling of the inguinal glands upon the same side as that of the puncture sometimes occurs, due, probably, to the penetration of the infectious material into the abdominal integument during the act of puncturing. The peritoneum itself, both visceral and parietal layers, shows the presence of a large number of small tubercles, interspersed with occasional large ones; this being especially the case when the tubercle bacilli are injected in a fine emulsion. The great omentum regularly appropriates very large numbers of bacteria, and becomes the site of a moniliform arrangement of tubercles. When the tubercles are injected in very large numbers the omentum rolls itself up and forms a sausage-like mass filled with caseous material. Serous or sero-hemorrhagic exudates sometimes occur, but not regularly. The retroperitoneal glands are early involved, then the spleen and liver. It is interesting to observe the gradual advance of the process from the peritoneal to the pleural side of the diaphragm by means of the lymph-channels which perforate it; the tubercles arising in the diaphragmatic pleura, then appearing in the bronchial glands, and finally in the lung itself.

These results are in harmony with those of most authors, in so far as accurate data have been recorded. It is, of course, presupposed that the bacilli of human or of mammalian tuberculosis, and not those of the avian disease, have been employed. (See Parisian Cultures, pages 39 and 40.)

SIGNIFICANCE OF THE ABOVE RESULTS FOR HUMAN BEINGS.

From these experiments we may draw the following important conclusions, which hold good also for human tuberculosis.

1. Tubercle bacilli which have invaded the organism regularly develop at the site of invasion, or in the next set of lymph-glands (law of localization). The glands act at first as a filter and arrest the progress of the bacilli. Cohnheim and Koch had already drawn attention to this relationship between the site of invasion and the localization of tubercle bacilli.

2. The further dissemination is gradual, so that the pathological findings ordinarily furnish a clue to the site of invasion.

3. Tubercle bacilli are capable of penetrating a macroscopically uninjured mucous membrane, in rare cases even the skin, especially if they are brought into close contact therewith by inunction. The author's contention of the viability of uninjured skin was demonstrated by histological findings as applying also to the gut by Dobroklonski, and to the larynx by E. Fränkel, who says: "The conclusions drawn by Cornet from his animal experiments find immediate confirmation in human beings. The absence of epithelium cannot be regarded as an essential prerequisite for the penetration of tubercle bacilli into the tissues.

As the author has frequently proved by demonstrations of animal preparations (including that at the Surgical Congress in 1889), we are now forced to abandon the theory of Bollinger and Schmidt that the tubercular virus cannot gain an entrance into the body after a simple cutaneous inoculation. This conclusion, which was based upon a series of negative experiments, was extended by Baumgarten, and the possibility of tuberculous infection through the skin or the mucosæ, if intact, absolutely denied. Such, however, is certainly not the case.

4. It is not requisite that the tubercle bacillus should go on to development at the site of inoculation. It may traverse the mucous membranes, and, in exceptional cases, even the skin, and leave not a trace behind. The next succeeding lymph-glands, however, cannot as a rule, be passed over without the production of some typical pathological changes, even though these be slight in character.

Recently Baumgarten has succeeded in repeatedly eliciting tuberculous disease of the skin by means of rubbing pure cultures of the bacilli into cutaneous wounds. The macroscopic appearance was far more like the so-called anatomical tubercle than it was like the lupoid diseases. Baumgarten, therefore, holds that the former disease may originate from a direct inoculation, the latter not.

5. The contradiction of the general belief in the immunity of certain structures, *e. g.*, the conjunctiva, the tongue, etc. All the organs above detailed show tuberculous changes, if brought into suitable contact with the organism.

6. The theory of a special predilection on the part of the lung for the tuberculous poison finds no experimental confirmation. The lung is first involved and shows the most advanced changes only in cases in which the infection travels by the air-passages; it is the organ last and least invaded in cases in which it is furthest removed from the primary site of infection.

Logically, it is entirely unjustifiable from the frequency of tubercular alterations in the various organs to draw inferences as to their predisposition for the arrest and development of tubercle bacilli (Bollinger). The degree of frequency depends not upon an inherent peculiarity of the organ, as the expression "predisposition" would seem to indicate, but upon external conditions; it is controlled by the distance of the organ from the site of infection, and upon the mode of infection, and it lies in the power of the experimenter to alter it at will. The statement is therefore just as fallacious as though one were to say that the penis is more predisposed to syphilis than the buccal mucous membrane. The fallacy of this conception is very evident from the contradictions between the various conclusions based upon it; since, for example, in those cases in which infection was set up by inhalation the lung would have to be regarded as the most predisposed of the organs, whereas when infection proceeds from the toe or the peritoneum, it would hold the position of the least predisposed. The greater frequency of tuberculosis of the glands is based essentially upon the fact that in every manner of infection these structures are next in proximity to the site of infection. Baumgarten, who maintains a special predisposition on the part of the lung, comes into conflict with his own theories when he records as a result of his feeding experiments that rabbits which partook only once of a small portion (50 to 100 cc.) of milk mingled with considerable numbers of bacteria developed unexceptionally a perfectly classical tuberculosis of the intestines, mesenteric glands, and liver, within ten to twelve weeks. The lung in these cases was not involved.

Apparent contradictions to this law of localization are brought into harmony with it by more accurate investigation. When, for example, Tappeiner fed dogs on tuberculous sputum, these animals became sick of a pulmonary instead of an intestinal tuberculosis. Further feeding experiments resulted negatively, and more accurate inquiry revealed that the first set of animals had accidentally been exposed to inhalation tests with tuberculous matter.

7. While infection through the vascular channels produces a fairly equal distribution of the tubercles among the internal organs, all other modes of infection, either proceeding from the skin or from the mucous membranes, are associated with a gradual advance of the process through the rest of the body. In other words, infection does not proceed, as a rule, by the blood-channels in animals, as is frequently asserted, but by the lymph-stream. It advances also through the tissue spaces, as is shown by its twofold method of progress, namely, to a certain extent in a direction opposed to that of the lymph-stream, as well as with it. The assumption of a hematogenous distribution, as primarily exemplified in the general miliary tuberculosis of man, is to be embraced only when the tubercles are found in various organs at the same stage of development. Furthermore, upon the lymphogenic propagation may be superimposed, in the course of the disease, a hematogenous advance.

PARALLELISMS BETWEEN SPONTANEOUS (HUMAN) AND EXPERIMENTAL (ANIMAL) TUBERCULOSIS.

A comparison of these experimentally determined conditions, especially their earlier stages, and the various forms of human tuberculosis cannot fail to reveal their resemblance in all essential details. Are not the alterations consequent upon the intravenous injections identical with the acute general miliary tuberculosis of human beings —with this exception, naturally, that in the latter ordinarily one can discover an older primary focus from which rupture into the vascular channels has occurred? Are not the intestinal changes which follow upon feeding experiments in every way similar to the various stages of isolated and of combined intestinal tuberculosis in men? The conjunctival, the corneal, the oral, the genital, the dermal forms of the disease—do they not resemble more or less perfectly the similar diseases which occur not rarely as primary affections among men?

The gland disease, also, which was produced upon one or both sides, after infections originating either in the nose, the mouth, the penis, or the vagina, coincides with the gland diseases grouped as tuberculosis.

Between the pouch-like cavities of the consumptive and the miliary tubercles consequent upon experimental inhalations there exists a certain difference. This difference is not, however, very profound in nature, but depends largely upon the fact that the rapid distribution of the bacilli in the guinea-pig destroys life before the pulmonary tubercles can form conglomerations and give rise, by their disorganization, to cavities. Moreover, the animals do occasionally develop small cavities, especially in cases in which the inhalations are not great in amount, whereby, of course, the progress of the disease is impeded.

Even the cheesy pneumonias, the usual absence of which in inhalation experiments would seem to argue against the identity of spontaneous and experimental tuberculosis, are now and again discovered in the animals. We are also in a position to produce it artificially if we imitate the causative factors at work, namely, the aspiration of cheesy masses by the injection of such masses or of sputum into the trachea and bronchi. Further, human infection is largely modified during its prolonged course by the admixture of a secondary infection.

The only real difference, namely, that in experimental conditions the spread of the disease from a single focus to the other organs of the body is more rapid than among human beings, is by no means constant. Rapid generalization of the disease is by no means rare in men; and the *genus homo sapiens* does not react in the same manner in all the stages of its life-history. It is a well-known fact that during childhood and youth general miliary tuberculosis is very prone to succeed upon any given tuberculous focus; in other words, that the immature organism evinces a fairly close resemblance to the laboratory animals, which also have an age of, at most, one or two years.

Conclusions.—There is a marked analogy between the pathological changes consequent upon the various modes of infection in animals and the clinical and pathological pictures of the disease in man, and this would seem to indicate that in the latter the infection had followed the same course. Such an interpretation is really forced upon us, in view of the numerous and reliable clinicals case in which a certain definite portion of skin or mucous membrane, intact or injured, came into contact with tuberculous material, and in which after the lapse of a certain length of time, the incubation period, the same typical tuberculous changes were provoked as in the experimental animals.

DIFFICULTIES IN DEMONSTRATING THE SOURCE OF INFECTION.

If only a few bacilli force their way into the body, as is mostly the case when infection occurs naturally, a considerable length of time intervenes before the tissue changes which they set up become sufficiently extensive to make themselves evident in one way or another. It is therefore far more difficult to ascertain the source of infection in tuberculosis than, for example, in cholera, anthrax, typhoid, or scarlet fever, in which the disease ordinarily declares itself within a few hours or days after the infection. It is this circumstance which makes plain why the infectious nature of tuberculosis was so long a matter of dispute; for who could recall, after weeks or months had elapsed, the conditions which determined the primary infection?

It is self-evident that infection by tangible objects, such as a corpse, or sputum, or handkerchiefs soaked with sputum, is more likely to strike the laity and to be recalled by them than is infection by the atmosphere permeated with invisible germs. An additional and important factor is that infection of the former character is especially prone to attack the skin, the external coverings, or the external openings of the internal body-cavities; in other words, situations upon which even slight tubercular changes are soon discovered and brought to the notice of a physician. And since such infections are often associated with traumatisms, which serve to fix the occasion in the memory, it is very easy to see that the source of infection is then easy to determine.

It is much more difficult, on the other hand, to determine an infection caused by food. For how very few are cognizant of the source of their food, of the meat or the milk, if we exclude chance contaminations of their slight practical importance; how much more difficult it is, also, to discover a source months afterward when the intestinal infection is finally diagnosed.

Great, and indeed often insuperable, difficulties attend the detection of infections by means of invisible germs in the air. In such cases one cannot hope to accomplish more than to determine that the patient sojourned in an atmosphere laden with bacteria—that is, in the immediate environment of an uncleanly consumptive—at a time which probably marked the beginning of the infection.

The source of infection also remains obscure, in case of an organ like the genitals, where the patient has every reason to deny the circumstances.

Taken all in all, however, when a primary and isolated infection arises in an organ connected with the exterior, are we not compelled logically to ascribe it to an infection from without? An autochthonous origin lies entirely outside of the pale of probability, and an intra-uterine transmission of the disease is excluded by the localization. Such cases of primary tuberculosis have been recorded in all the organs communicating with the exterior; their number has increased with our more accurate methods of examination, and stands, as may be seen, in direct proportion to the chances of infection to which the organ is exposed.

FACTORS WHICH FAVOR OR HINDER INFECTION.

One must not conceive of tuberculous infection as of such nature that wherever a bacillus comes into contact with an organ localization and proliferation with tubercle formation must necessarily occur. It is rather dependent upon a set of conditions which (excluding the constitution of the organism as a whole, ordinarily called the "idiosyncrasy") are comprised by the histological character of the tissue, by the nature of the infectious material, and by the closeness of contact between these two.

Thus, the bacillus lacks the conditions favoring its development upon intact normal epithelium. Likewise, the epithelium of the mucous membranes does not easily permit proliferation, although the various tissues differ in this regard according to the character of the cells. Squamous epithelium is in every way firmer than the delicate cylindrical epithelium, and resists the invasion and development of bacteria far more effectually. But the normal mucous membrane gives additional protection from a coating of mucus, which, even if ever so thin, shields it from direct contact with the bacillus. This mucus does not remain fixed in position, but has a physiological tendency to seek the mouth of the organ, and so carries with it the bacilli, which lie as though upon the surface of a current. Many mucous surfaces, moreover, are provided with ciliated cells, which determine the direction of this stream and accelerate its speed. The more active the secretion of mucus and the more swift the current, the more rapidly is the bacillus eliminated, whence, by reason of the slowness of its growth, it fails to secure sufficient time to multiply in the tissues. This is more especially true if the organism has been deposited at no great distance from the surface opening, and the space to be traversed consequently is relatively short. The chemical qualities of the secretion poured out from some of the mucous membranes and from certain specialized glandular apparatus is perhaps capable of restricting to a certain extent the proliferation of the bacteria. Bactericidal properties have been attributed to the nasal mucous membrane (Wurtz and Lermoyez), the vaginal secretion (Menge, Gow, Krönig), and the lachrymal secretion (Valude, J. Bernheim), and the attempt has been made to establish these contentions experimentally.

The nature of the infectious matter is of essential importance. A single bacillus is swept away with comparative ease because of its insignificant weight; but bacilli generally become united into considerable colonies, thanks to their content of mucin, and to eliminate these is far more difficult for the organism. One is often struck by the fact that in these minute affairs the same physical laws of gravity maintain as in the vast economy of nature; and that here, where the question is one of thousandths and millionths of a milligram, a fraction thereof plays the same important rôle as do grams and kilograms in larger spheres. If live bacilli are commingled with dead ones in these aggregations,—and we know that in sputum the majority are dead,—the dead forms exercise a more rapid and intense action, by means of the diffusion of their chemical matters, than do the live organisms with their slow process of proliferation. The chemical irritation leads to inflammation, and gives rise to increased secretion when an open canal leading to the mucous surface is involved. This, again, is a factor in the elimination of the bacilli *per vias naturales*. In the interior of the tissues, on the other hand, a protective wall against the further advance of the increasing bacilli is formed by a heaping up of leucocytes. Thus, in both cases, infection of the body may be avoided.

Whether there is also a difference in the *virulence* of bacteria in the true sense of the word has not yet been determined. If such be the case, these differences are also factors of importance (see page 50). Finally, the mode of infection plays a very great rôle. When the bacillus comes into surface contact with an uninjured epithelium, it has only a slight chance of gaining a foothold. When it comes into more intimate contact, it may under certain circumstances force its way down deeper and become domiciled. Thus it happens that when tuberculous material is thoroughly rubbed in, the bacilli are able to penetrate the squamous epithelium of the mouth and the vagina, and into the cutis itself, even though these surfaces be absolutely free from visible injury.

These variations which occur among normal organs are naturally intensified when pathological processes destroy the continuity of the tissues, or otherwise alter them, or modify the quality and quantity of the secretion. Thus, injuries or inflammations may deprive the skin or the mucous membrane of its epithelial covering and thus open wide the gate to bacilli, and stagnating secretions may further their development. On the other hand, profuse secretions may interfere with the localization of the organisms and hasten their elimination.

Due regard for all these factors and proper estimation of their importance will make it clear to us why a tuberculous focus arises in one place and not in another, and why a bacillus gains a foothold in one particular area, while the broad interval which it was compelled to traverse in order to reach this destination remains unaffected.

We must now pass to the clinical data regarding infection of the various organs.

CLINICAL DATA CONCERNING THE INFECTION OF VARIOUS ORGANS.

INFECTION OF THE SKIN.

Tuberculous disease expresses itself in various ways, such as tuberculous ulceration, tuberculosis verrucosa cutis, anatomical tubercle, scrofuloderma, etc. The most frequent form is lupus, the identity of which with tuberculosis proper is firmly established, notwithstanding certain clinical differences. Its tuberculous origin was *à priori* probable from its frequent association with other forms of tuberculous disease, from its repeated occurrence in connection with tuberculous fistulæ, and also from its histological characteristics. All doubt was removed after it was shown that tubercle bacilli could be demonstrated in lupoid tissue, that they could be grown therefrom in pure cultures, which, again, were capable of giving rise to tuberculous disease. Furthermore, the tuberculous character of the disease is betrayed by the presence of the typical tuberculin reaction, and by the unmistakably tuberculous nature of the secondary changes, such as those involving the glands, the inoculation of which produces tuberculosis, as the author has repeatedly shown.

The tuberculous diseases of the skin illustrate most distinctly the genesis of the processes. In itself, the skin is not very favorable to the development of tubercle bacilli; since the temperature requisite for their growth is afforded by but few places and at occasional times. In addition, the uninjured epidermis affords a fairly reliable protection, so that the simple pollution with tuberculous sputum does not suffice to produce infection. This is more especially true of localities in which thickening or callosities have been formed, as the *palma manus* or the *planta pedia.* Places which are most effectively protected from direct contact by means of a thick covering of hair, such as the skin of the head, are only exceptionally the seat of tuberculosis. This is also rare in places covered by the clothing, although it is true that here the increase in local temperature would favor the development of the tubercle bacilli. This localization of tuberculous lupoid disease in the vast majority of cases upon areas exposed to free contact affords a very powerful argument for its exogenous origin. Thus, according to Raudnitz, of 209 cases of lupus 65.6 per cent. involved the nose, lips, and angles of the eye, and 24 per cent. the trunk and extremities; according to Hahn, of 424 cases of lupus only 105 (24.8 per cent.) involved the extremities, but in only eight of these was it restricted to those parts, while in 44 of these 105 cases the face was the first to be attacked. According to Gramm's statistics, for 573 cases of lupus involving unprotected areas of skin, there were only 62 cases involving covered parts.

More important is a series of clinical cases which give more or less definite evidence of a primary exogenous infection, and which for the most part involved areas previously sound in persons without hereditary taint.

Thus, for example, injuries received at the autopsy of tuberculous corpses have repeatedly given rise to local tuberculosis (anatomical tubercle), and, in some cases, to secondary swelling of the glands, tuberculosis of the lung, and finally death. Such cases have been recorded by Verneuil, Verchère, Pick and Pfeiffer. It is well known that Laennec attributed his phthisis, to which he eventually succumbed, to an autopsy wound.

Gerber has described with special care his own case. He wounded his finger during the autopsy of a consumptive, and, in spite of quick disinfection, there developed at the site of the injury a nodule of the size of a cherry. Within four months the axillary glands were also involved. Extirpation resulted in cure.

That such observations are not more frequent is not to be ascribed to the absence of predisposition on the part of the injured person. In part it is due to the fact that tuberculous bodies are ordinarily infectious only at the actual site of the disease and not through the blood and the body-fluids. In addition, the infectious material is often satisfactorily removed from small wounds by a physiological process of cleansing,—namely, bleeding,—which serves to diminish the danger from incised wounds, when present; this is reinforced by thorough scrubbing, which no anatomist would neglect to perform. That these factors are of importance has been proved by experiments of the author.* Such autopsy wounds are generally limited to persons who have already passed their youth, and in whom, as has already been explained, the infectious material is apt to remain localized at the site of infection. (See chapter on Predisposition, Age.)

Animals also frequently give rise to such infections. Thus, as L. Pfeiffer relates, a veterinary surgeon developed a cutaneous tubercle as the result of the autopsy of a tuberculous cow, and died one and one-half years later of pulmonary consumption. A similar infection in the case of a powerful, healthy, butcher's apprentice resulted only in the formation of a tuberculous ulcer, with subsequent lupus of the arm and infiltration of the lymph-glands, which latter were not to be palpated (Jadassohn). Braquehaye had under treatment a slaughterer, in whom a number of fissures in the skin over the wrist-joint became the site of a tubercle. The form of tuberculosis of the skin described by Riehl and Paltauf, tuberculosis verrucosa cutis, was most often found by them in individuals who had much to do with animal products, such as butchers, coachmen, inn-keepers, and cooks. They found it in places most exposed to contact with such material, namely, the tender dorsum of the hand, the extensor surface of the fingers, the interdigital folds, and more rarely on the tough palmar surface and the neighboring areas of the forearm. The foregoing cases afford a curious commentary upon Bollinger's dictum, that the manipulation of tuberculous organs may be carried on with impunity so far as the danger of an infection of the skin is concerned. Opportunity for infection is afforded especially in the case of tuberculous individuals and the intercourse with them. A domestic wounds herself with the broken sputum cup of a consumptive and falls sick of local tuberculosis, with swelling of the axillary glands (Tscherning). Similar cases are recorded by Merklen, Lesser, and Holst. A child strikes its head in falling upon a chamber-pot used as a receiver by a tuberculous mother; the pot breaks, giving rise to injuries which at first heal, but secondarily break down; the child develops a localized tuberculosis with swollen cervical glands, and finally succumbs (Deneke). Verchère, Jeanselme and Leloir observed cases in which the bite of a consumptive gave rise to typical local sequelæ. A woman of forty years tending a very sick consumptive acquired a slight abrasion of the index-finger; a tuberculous ulcer and tuberculosis verrucosa cutis soon developed at the site of the injury. A consumptive was careless with his sputum and had the habit of wiping his mouth on a towel used by his wife also; his wife rubbed her nose with one of these contaminated towels, and from this slight injury proceeded a slowly advancing lupus (Winfield). A sick nurse wounded her hand upon the bed of a consumptive; the insignificant but sluggish wound became the site of a tuberculosis verrucosa cutis (Thibaudet). A woman of thirty-two years and without hereditary taint developed tuberculosis of the face as a result of associating with a tuberculous friend, whose frequent spells of coughing often threw particles of mucus into her face (Corlett). A student who was associated with the clinic in the capacity of sputum examiner scratched his head with his infected fingers and developed lupoid granulations (Wolters). In the case of another physician who was much occupied in the consumption ward, an ordinary furuncle gave place to a tuberculous ulcer (Avendano). An orderly who injured himself with a splinter while polishing the floor of a ward acquired a tuberculous abscess (Tardivel), while in another similar instance a tuberculosis verrucosa cutis was the result (Sanguinetti). Two individuals who walked with their bare feet about a floor which was in all probability soiled with tuberculous sputum, developed in the one case lupus (Gevaert), in the other verrucous tuberculosis of the skin (Brugger).

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* Five animals were treated in the following fashion: Superficial injuries were inflicted upon the back; tuberculous material was then brought into contact with the surface and the part thoroughly cleansed and disinfected. Four animals became diseased, but one was saved by the process of cleansing.

In the washing of the soiled clothes, particularly of handkerchiefs soaked with sputum, tubercle bacilli are in a measure rubbed into the hands. Nevertheless, the danger is not very great, since the germs are again washed away by the soap and the large quantities of water used. Yet cases of infection through this means are recorded by Steinthal, Dubreuilh and B. Auché, Bowen, v. Eiselsberg, and Leloir.

A girl who frequently made use of her sister's handkerchief soaked with sputum developed a lupus of the nose (Leloir); and a similar case is recorded by Baginsky. A punctured wound which was bandaged by a contaminated handkerchief was followed by an anatomical tubercle (Raymond).

V. Düring, Unna, and Leloir make mention of girls who wore the earrings of consumptives, and thus acquired a progressive tuberculosis. In case of tuberculous eruptions about the ear, one would have to think further of an infection through energetic kisses and caressing bites, such as Zucker and Mracek have described for syphilitic sores similarly located (cited by Zucker).

Operation wounds in non-tuberculous individuals are not especially prone to infection, for the hemorrhage and the antiseptic cleansing serve to wash away chance germs which lodge upon the surface; purulent secretions accomplishing the same end. But, neglecting all these factors, we must not think of tubercle bacilli as floating freely and ubiquitously in the atmosphere; as has already been shown, there is reasonable fear of danger only in the immediate neighborhood of an uncleanly consumptive; and cases of such infection are correspondingly infrequent. Infection associated with ritual circumcision is treated of in connection with genital tuberculosis.

An operation wound in a case of Kraske's was apparently infected through the tuberculous sister of the patient, in a case of Wahl's through a nurse afflicted with lupus, in a case of Tuffier's through a tuberculous bed-mate. Similar cases are recorded by Middeldorpf and Verneuil.

Small wounds which scarcely bleed or attract any attention more readily permit of the settling of bacteria, if the conditions be favorable. Transmission of syphilis by means of luetic saliva which is rubbed in during the process of tattooing is well known. Barker records that twelve soldiers of one regiment were infected in this wise by a syphilitic; and a lupus developed in a strong and healthy girl upon an area into which phthisical saliva had been rubbed during the process of tattooing (Jadassohn). A youthful consumptive shortly before his death tattooed two brothers and a friend in the arm, and rubbed his saliva into the wound. In all three cases numerous pustules were found, with secondary swelling of the cubital and axillary glands. Microscopically there were indeed no tubercle bacilli, but giant cells were present (Colling and Murray).

Often it is the case that the fact of a tuberculous infection of a given wound may be established while the source itself remains undetermined, as, for example, in burns (Solger), skin transplantations (Czerny), stab wounds (v. Eiselsberg), and cuts (Leser). Wolters observed a lupus consequent upon a wound from a pitchfork.* Riehl described a wound of the thumb which healed at first, but subsequently became the seat of two pea-sized nodules of tuberculous nature. Sherwell observed a case of tuberculosis verrucosa cutis upon the dorsum of the thumb in a man forty years old following upon an injury.

Lupus or lupoid changes have been found upon vaccination scars (Besnier, Demme, cited by Förster), at the site of morphin injections† (König and v. Eiselsberg), upon cupping scars (Leloir), in the puncture for an earring (Sachs, v. Eiselsberg, Jadassohn), upon a wound of the auricle produced in cutting the hair (Bloch).

Infection proceeding from eczematous areas was first described by Demme. A girl developed caseous retromaxillary glands and tuberculosis upon an eczema of the scalp. A healthy boy with eczema over the abdomen was infected in this area by his tuberculous mother, whereupon he fell a victim to abdominal tuberculosis (Demme). A case of tuberculosis of the cubital glands following upon eczema of the hand had been recorded by A. von Volkmann; in this latter case tubercle bacilli were found.

In Thüringia, according to Wahl, excoriations are washed with new milk, in many parts of France with fresh cream; in these places infection may be caused if cattle tuberculosis be at all widespread. Leloir publishes such a case of a farmer's wife who in the bloom of health developed a lupus at the site of the wound.

A tuberculous mother dressed a chronic eczema in a child with bread which she had chewed, whereupon lupus developed in the area of the disease (Leloir). Again, lupus developed in a wound which was daily dressed with court-plaster moistened with the saliva of a tuberculous nurse (Leloir). The foolish custom of rubbing wounds, especially those of children, with saliva, or of breathing upon them, is widespread, and the infrequency of consequent infections is only to be attributed to the fact that the saliva of the tuberculous, in contrast to their sputum, rarely contains bacilli.

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* Possibly from excretions or secretions of tuberculous men or animals upon the dung heap.

† The morphin syringe had been used for a long time upon a very ill consumptive.

A woman of forty-two years developed lupus of the face, of the buttocks, and of the labium majus; the patient had lice, and evidently the tubercle bacilli gained an entrance through the numerous excoriations produced by scratching (Lipp). Under similar circumstances a case of Jadassohn developed the picture of a tuberculosis verrucosa cutis (no traces of internal tuberculosis being present).

Just as eczema paves the way for lupus, so too it may afford a soil for carcinomatous changes (Lewin, Winternitz, and others).

In the series of cases detailed above, wounds play a great rôle in rendering possible the invasion by tubercle bacilli. In the same way, inflammations, erysipelas, coryza, the tender epithelium over recent scars, further scratch marks in scabies, and contused areas, all afford conditions favorable to the localization of germs. It would be going too far, however, to consider such lesions of tissue as a necessary antecedent to cutaneous infection. Although passing contact of tuberculous material with the skin is ordinarily insufficient to produce infection, yet with thorough inunction the macroscopically uninjured skin constitutes no barrier to the invasion of the bacilli. This is deducible by analogy from the experiments of Garré, Schimmelbusch, Roth, and Wasmuth with other bacteria, and has also been proved directly for the tubercle bacillus by the experiments of the author; moreover, certain of the clinical data above recorded give it direct confirmation. According to Wasmuth, the space between the hair-shaft and the sheath gives the portal of invasion to the bacilli, while the sebaceous and sweat glands are not favorable to infection.

The prominence of injuries in the casuistry is to be explained by the fact that they often furnish the only tangible explanation for the origin of an infection.

If there is already a tuberculous focus elsewhere in the body, the skin is also predisposed to infection, especially if the secretion from the diseased area is profuse; hence it is that skin tuberculosis (lupus) is frequently found combined with older foci, especially in the lung, although former writers have denied this. Besnier found that of thirty-eight afflicted with lupus, eight, or 21 per cent., had pulmonary tuberculosis, and Leloir found that of 312, ninety-eight, or 38 per cent., were in this condition. Among the 144 cases of lupus studied by Block in the Breslau dermatological clinic, more than three-fourths (79 per cent.) suffered from other forms of tuberculous disease, and of these one-fourth had suffered previously to the onset of the skin disease. Sachs determined the presence of other forms of tuberculosis in sixty-six, or 62.3 per cent., out of 105 cases of lupus; and of these sixty-six, thirty-six were tuberculous before the onset of the lupus. Renouard in eighty-seven cases of lupus found other tuberculosis thirty-three times. Haslund found a combined tuberculosis in 60 per cent. of such cases. Bender in Bonn found in 159 cases of lupus (Doutrelepont's) evidence of a combined tuberculosis in 99, or 62 per cent.

The preference of tubercular foci for the neighborhood of the mouth and anus (Doutrelepont) indicates clearly their genesis from sputum and feces. Vallas, in thirty-three cases of skin tuberculosis, had thirteen which were localized at the anus, and fourteen at the lips. Ritzo determined a similar ratio.

Ehrlich found a tuberculous ulcer of the lip in a consumptive, following upon local injury. According to Behrend, a certain individual who for years had suffered from tuberculosis of the lungs and the larynx was bitten by a mosquito and developed a lupus proceeding from the area of scratching. In a consumptive of Epstein's a burn was followed by a tuberculosis verrucosa cutis on the dorsum of the thumb. Nielsen described the case of two consumptives who were accustomed to wipe their moustaches after expectoration with the dorsum of the hand, and who thus developed lupus at that site. A similar case of Arning's had the same cause (tuberculosis verrucosa cutis upon the dorsum manus of a consumptive of thirty-two years), and Vidal attributed to this habit the fact that in consumptives the dorsum of the hand furnished a favorite site for this lesion.

Tubercular foci are often to be found in connection with fistulæ and incisions which communicate with tuberculous glands, bones, or joints (Renouard, Block, Gramm, Nielsen, Rayet, Riehl); often they arise even after cicatrization has begun (Cronier). The latter circumstance is probably owing to the fact that the tubercle bacilli were washed away as long as the secretion remained profuse, and that only after it had decreased could they remain fixed in the proximity of the opening, and so go on to development. The fact that this origin of fresh tubercular foci coincides in time with the healing up of others does not speak for a preëminent influence on the part of idiosyncrasy. After an amputation for tuberculosis of the knee-joint Riehl observed large nodules and vegetations upon the stump, which he described as fungus.

A special significance attaches to the question whether tuberculosis can be transmitted by vaccination. The possibility of inoculating syphilis by this means is undoubted. Not in every instance in which a local syphilis follows upon vaccination is the vaccine itself to be accused, since this has occurred in cases in which animal lymph, by no possibility infectious, was employed (Rosenthal and Haushalter); infection in such a case being evidently attributable to uncleanly instruments. An actual syphilitic vaccination seems, however, to have occurred in a case recorded by Gallia, in which a physician took the lymph from a syphilitic child, and thus infected thirty-five others.

In tuberculosis the conditions are absolutely different from syphilis, inasmuch as in the latter disease all the fluids of the body have an infectious quality; whereas in tuberculosis, the disease being more or less limited, the agents of infection, the bacilli, are ordinarily absent from the blood and the lymph except only in the general miliary type of the affection. Cows and calves with miliary tuberculosis need not be considered sources of vaccine. *A priori*, therefore, transmission of the tuberculous virus by vaccine is not to be considered; experiment and clinical experience are in full accord with this conclusion.

L. Meyer failed to find tubercle bacilli in the secretion of the pustules of eleven consumptives; similarly, the lymph was regularly found to be sterile in the consumptives vaccinated by Acker. In fact, there exists no single well-authenticated case of such an infection. It is, of course, not to be denied that a vaccination wound, just as any other, may be infected by tubercle bacilli if they be carried into it; but an infection of this character, which is entirely independent of the vaccine itself, can hardly be called a "vaccination tuberculosis."

Lymphogenous Infection.—In addition to inoculation from the exterior, we must not forget that tuberculous disease may be carried to the skin by the lymph-channels, especially from a neighboring focus in a mucous membrane. Neisser is inclined to ascribe the derivation of most cases of facial lupus to the mucous membranes, a conception which finds some support in the data collected by Bender from Doutrelepont's material. He found among 380 cases of lupus, 173 of lupus of the mucous membrane, of which 75 involved the nasal mucosa, 4 the conjunctiva, 6 the nasal duct, 25 the lips, 31 the gums, 1 the tongue, 13 the larynx, 1 the rectum and external genitals.

The **hematogenous infection** of the skin, as conceived by Baumgarten, is very rare; at least reliable records thereof are extremely scarce. Most indicative of such an origin are multiple tuberculous foci variously situated upon the body, as described by Heller, Goldzieher, Doutrelepont, P. Meyer, Leichtenstern, and O. Naegeli. The infrequency of miliary foci in the skin as a part of general miliary tuberculosis is probably due to the comparative coolness of the skin, which inhibits the growth of the bacilli; thus death brings an end before any notable changes make their appearance upon the skin.

INFECTION OF THE INTESTINAL CANAL.

Tubercle bacilli gain an entrance into the body by way of the intestinal canal in various fashions. They are carried in with the air of inspiration, in mouth-breathing; by dirty objects which children, especially, bring to their mouths, as in sucking their fingers, chewing on dirty nails, pen-holders, or toothpicks; by kissing tuberculous individuals, but especially are they carried in by food which is derived from infected animals or which accidentally becomes contaminated.

Infection of the Mouth and the Pharynx.—The occurrence of tuberculous disease in the buccal cavity has been known for some time. Schlieferowitsch gathered about ninety such cases from the literature previous to the year 1885, and some of these go as far back as Morgagni. This list has since then gained considerable additions, since Orlow, and especially Michelson, drew attention to it afresh.

The oral cavity in this species of infection is the first stadium of the tubercle bacillus, yet is itself only rarely affected. According to Heller, of 8000 patients of a laryngological polyclinic only four or five had buccal tuberculosis. Apparently the mouth does not afford the conditions necessary to the growth of bacilli. It is true that innumerable micro-organisms occupy it,—Black, Vignal, and Miller have described an entire flora,—but this luxuriance is owing to constant importation of fresh germs through the air and the food rather than to their proliferation upon the spot. Just as the oral mucus inhibits any pronounced growth of the pneumococci and the gonococci, so too it cannot fail to evince its bactericidal properties upon tubercle bacilli.

The larger number of germs that are taken into the mouth are rapidly mixed with saliva, in the same manner as is food, and thus they are kept from direct contact with the mucous membrane, and are eventually either expectorated or swallowed. Their favorite lurking places are in hidden corners, as in the sulcus between the gums and the lips.

The squamous epithelium of the mouth, when intact, affords a barrier against the invasion of the bacilli into the mucosa which is very efficient, far more efficient, indeed, than the very vulnerable ciliated epithelium of the respiratory tract. Thus Roth found it possible to infect rabbits by rubbing Ribbert's bacilli over the nasal mucosa, while the mucous membrane of the mouth resisted the invasion. In the course of years the epithelial stratum of the mouth becomes thicker and more resistant by reason of the continual friction to which it is exposed, in the same manner as do the external skin and the vaginal mucosa.

That the injured oral mucosa affords no absolutely impassable barrier against the invasion of tubercle bacilli has already been demonstrated in the description of the author's experiments (page 100).

Injuries or defects of the mucosa naturally facilitate the immigration and localization of tubercle bacilli. Thus tuberculous ulcers of the lips, the gums, and the cheeks occupy by preference places previously wounded or excoriated.

In addition to purely mechanical injuries, pathological processes, such as simple catarrh, inflammations, eczema (eczema of the tongue), psoriasis, etc., prepare the way for tuberculous infections. The occurrence of tuberculous affections upon syphilitic foci is a result of the ulceration and loss of substance produced by the latter disease. Wagner described tuberculosis of the soft palate in two previous syphilitics, and Agnanno the tuberculous infection of a luetic ulcer of the velum palatinum.

Moreover, the continuous action of irritants predisposes to the development of tuberculosis. Certain authors are inclined to ascribe some influence to alcohol and tobacco (Tusseau); thus, B. Thompson saw a tuberculous ulcer running from the base to the tip of the tongue along the left margin, in association with a psoriasis linguæ, the patient being a consumptive aged fifty-one, and a heavy smoker. The greater the number of tubercle bacilli carried into the mouth, the greater is the probability that some of them will find an open gateway. Therefore it is self-evident that consumptives, who are continually exposed to such infection through their sputum, are the most frequent victims of oral tuberculosis.

Yet even in phthisis, despite the amount of sputum and the apparent existence of a predisposition, tuberculosis of the oral cavity is a comparative rarity. This appears to be due to the fact that the tubercle bacilli and the cheesy fragments become covered with a coating of mucus in their course from the bronchi to the mouth, and so do not come into direct contact with the mucous membrane of the mouth. We take cognizance of the existence of this external layer of mucus when we cleanse the sputum of it, with its accompanying germs, by washing, in order to get at the bacteria of the pulmonary cavities which lie within.

Secondary tuberculosis of the mouth in consumptives being rather infrequent, the primary disease in otherwise healthy individuals is *à priori* much rarer, since the opportunity of getting at the buccal mucous membrane is not often granted to the bacteria.

Generally, oral and pharyngeal tuberculosis appears as an eruption of isolated or confluent nodules, the latter often assuming the guise of an infiltration; the subsequent course being marked by ulceration. In other cases, especially such as are carried by proximity, lupus takes the more superficial and therefore benign form, although in its ulcerated condition it presents no characters differing essentially from tuberculous ulcers. In the tongue, also, situated in the parenchyma, are certain more or less deeply rooted tumors which are subject to confusion at first with carcinomata or gummata.

Lupus is especially frequent upon the lips, and attacks individuals in flourishing health, gradually invading gums and palate; but the cases of ulceration are rarer. Eichhoff described a tuberculosis of the lower lip in a consumptive, which gradually embraced the corner of the mouth, the upper lip, the tongue, and hard palate. E. Finger described tubercles in the sublingual glands. Other cases of labial tuberculosis are recorded by Bouchut, Plichon, Neumann, and others.

Tubercular changes in the gums, where, especially in the gingival folds, sputum and food-particles are prone to be retained, have been described by S. Solis Cohen; and in combination with a contact ulcer of the lip, by B. Baginsky, Hajek, and Giraudeau.

According to an observation of Jaruntowski, a cavity in a carious tooth belonging to a consumptive with gingival and palatal tuberculosis contained large numbers of tubercle bacilli lying in masses. A wound produced by pulling a tooth was the portal of entry for tubercle bacilli in a case observed by Doutrelepont. A painter had a cough for two years; after the removal of an upper molar the wound refused to heal, and discharged small splinters of bone, involving the entire alveolar process of the superior maxilla and also extending over the mucous membrane of the cheek. A consumptive patient of Schlieferowitsch had a carious tooth pulled, in order to give vent to the pus; suppuration continued and extended to the gum, which became the seat of a considerable tuberculous loss of substance. Neumayer described a similar case in a consumptive. The teeth seem often to be an indirect cause of tuberculous infection, inasmuch as small, prominent irregularities, such as are often found in caries, wound the opposite mucosa and so favor the invasion of bacilli.

Schlieferowitsch observed a tuberculous ulcer of the tongue which the patient attributed to trauma received from a sharp tooth subsequently extracted. Heymann exhibited a consumptive with a tuberculous ulcer of the cheek, which corresponded accurately in position with a bad tooth, extracted shortly before the appearance of the ulcer. A man with laryngeal tuberculosis, observed by Morel Lavallée, had tuberculous ulcers on the margin of the tongue, which were due apparently to the stumps of those teeth which still remained in the mouth. Mendel saw a tuberculous ulcer of the tongue which originated from the irritation of a sharp cusp on the first molar.

Even the mere pressure of the teeth seems to further the development of an infection. Thus a palatal tuberculosis became complicated by disease of the tongue at the site of the pressure marks of the teeth. Müller describes a tuberculous ulcer which began at the left angle of the mouth, and three months later had extended back parallel with the line of closure of the teeth; at the left apex was a beginning catarrh. A similar experience is recorded by Schlieferowitsch, case 5.

The tongue, by its intimate contact with tuberculous sputum, becomes especially disposed to infection. The margins which rub against the teeth and the tip are involved in the vast majority of cases; much more rarely the dorsum or the lower surface.

A secondary lingual tuberculosis in consumption has recently been described by Hansemann, Stewart, Bryson Delevan, Jakson, Poncet (in one case combined with tuberculous ulcer of the finger), Salzer, B. Baginsky, A. Fränkel, Charlier, Martin, Chauffard and Dardignac.

Further cases are described by Mollière, Feurer, James and Bruce, Lauschmann, Bruneau, Barth, Fleischmann, Dowd, Sabolotzki. Lupus of the tongue has been observed by Bender, Leloir, Miller, Michelson, Cheever and Darier.

"Concerning the occurrence of tubercles in the throat, little is known," wrote Wendt in 1874 in Ziemssen's "Handbook." But how matters have changed since then!

The tonsils, both by reason of their position and of their structure, assume a considerable rôle in tuberculous disease. The act of deglutition forces sputa or infectious food, as the case may be, into contact with these organs, which are especially fitted by numerous crypts and crevices to receive certain small particles. Dmochowski even credits the crypts with suction power, in such fashion that in deglutition they first express their secretion under the pressure of the constrictors, and then draw whatever portions of liquids or of sputum remain upon their surface into the crypts as they again relax and expand.

The epithelium of the tonsils is subject to frequent catarrhal inflammation, which serves to break it up and to cause it to desquamate. Outside of this, however, there is normally an uninterrupted emigration of numberless leucocytes, and the epithelium consequently becomes deficient and, indeed, almost sieve-like; thus the gate is opened to invasion, which would advance even more swiftly were it not that the opposing stream of leucocytes affords a barrier which is efficient at least against relatively small armies of germs. This defense is almost powerless, however, against the invading hordes of bacilli in consumption, and is overcome by them. Histological demonstration of tubercles in the palatal tonsils at autopsy has been made by Strassmann, thirteen times out of fifteen cases of pulmonary consumption, but not at all among six cases in which the lungs were free or only slightly affected.

Dmochowski found them in every one of fifteen cases of pulmonary tuberculosis, fourteen of which were in the advanced stage.

Schlenker found them in all of nine cases of pulmonary consumption of severe type in adults, eight being bilateral, one unilateral. He found them twice only in nine cases of consumption of mild type in adults, and three times in five cases of mild and medium type in children.

Kürckmann found them in all of eleven cases of pulmonary phthisis, mostly severe. They were absent in all of thirteen cases of chronic bronchial tuberculosis of long standing. They were absent also in one case of tubercular meningitis, but present in one case of healed bronchial tuberculosis.

The palatal tonsils were tuberculous in forty-eight out of fifty cases of generally severe phthisis, but only in six out of thirty-four cases in which the lung was only slightly or not at all involved.

Ruge found tubercles in the tonsils in every one of five cases of severe phthisis, twice *intra vitam;* among twelve other persons (anemics), including two with incipient phthisis, etc., the tonsils were in every case free. According to Dieulafoy, of sixty-one guinea-pigs in which he implanted pieces of the tonsils, eight became tuberculous.

In addition to these cases, the tonsils were found to be tuberculous in one case of pronounced food-infection, the lungs being free (Schlenker), and once in a diphtheritic child otherwise not tuberculous, that is to say, primarily (Krückmann). Orth also had previously described the occasional occurrence of tonsillary tuberculosis in diphtheritic children with intact lungs, and had also produced it in rabbits by giving infected food. Baumgarten produced it repeatedly by this latter means.

Recently Schlesinger has found tonsillary tuberculosis post mortem in twelve out of thirteen cases of florid consumption in children.

To resume: Where the opportunity for infection is given, by reason of the presence of large numbers of tubercle bacilli either in the sputum or the food, tuberculosis of the tonsils is frequent. In the course of severe pulmonary consumption it occurs almost invariably; in other cases it is exceptional.

The tonsils correspond histologically with the lymph-nodes, whose function, characteristically, is to take up and collect the tuberculous virus; they may themselves become diseased, but they stay the advance of the bacilli into other regions of the body for a time, and, indeed, often permanently. Therefore it is possible that the tonsils, despite the frequency of their infection, are to be regarded as a barrier, though perhaps somewhat inefficient, to defend this exposed portion of the body.

When large numbers of bacilli force an entry, the tonsils, while able to delay, are not entirely able to prevent the advance of the bacilli, as is evident from the simultaneous infection of the cervical glands in the case above described.

It is fallacious to conclude from this coincidence of tonsillary and glandular tuberculosis that tuberculosis of the cervical lymph-glands, ordinarily called scrofula, is almost always traceable to a preceding tonsillar infection. The frequency of such cervical infections secondarily to foci variously located on the head—*e. g.*, eczemas and nasal tuberculosis—points unmistakably to a multiple origin. To this matter we shall return in our consideration of glandular tuberculosis.

In the above-described species of infection, the tonsils are of normal size, atrophic or hypertrophic, and rarely betray their disease to the naked eye. Ulcerations such as Lublinski has described are unusual, and occur rather with the extension of a neighboring focus to the tonsils.

The sebaceous glands of the base of the tongue are identical in structure with the tonsils, and it is noteworthy that in his case Dmochowski found them to be similarly, although less constantly, affected (nine of fifteen consumptives). This diminished frequency he ascribed especially to the difficulty of access, the narrow openings—in short, to the slighter danger of infection.

The palate and the soft palate become tuberculous, according to Guttmann, in about 1 per cent. of the cases of phthisis in the hospital. Their exposed position brings this about; for in the act of coughing with open mouth, the velum palatinum is driven against the posterior pharyngeal wall, shuts off the oral cavity from the nasopharynx, and bears the brunt of the impact of the sputum driven up from the trachea. Swallowing movements also bring the sputum into close contact with the palate and the mucous membrane of the pharynx.

The inferior portion of the posterior wall of the pharynx, with its smooth surface and its rich secretion of mucus, does not afford conditions favorable to the growth of the tubercle bacillus, just as a much trodden pathway through a meadow does not permit of the growth of grass, notwithstanding that the soil itself is in proper condition. For here, too, there is an incessant to-and-fro motion, food and drink passing downward, mucus traveling upward, so that the bacillus is denied the chance to gain a firm hold. According to Lublinski, of 16,000 patients in the University Polyclinic only two or three presented pharyngeal tuberculosis; B. Fränkel found only one case of miliary tuberculosis of the pharynx among 1863 throat and nose patients; Boecker had 12 cases of pharyngeal tuberculosis among 2950 patients of this class; Kidd saw tuberculosis of the soft palate four times, of the pharynx six times, among 500 autopsies.

But in case one of the innumerable passing bacteria does actually succeed in forcing an entrance into the mucosa and multiplying therein, its further subepithelial development is highly favored by the massage-like pressure which is exercised upon the surface by the act of swallowing. The miliary form of the disease, which is so often met with here, may thus be induced and its malignancy favored. In severe phthisis when strength is on the ebb, when the patient apathetically retains the sputum in his mouth and expels it incompletely, tuberculosis of the palate and the tonsils occasionally inaugurates the last act in the disease.

Here, too, are to be mentioned the rare forms of tubercular retropharyngeal abscesses, caused by broken-down, cheesy lymph-nodes, which, possibly, are derived from infections of the nose by means of the tributary lymph-channels draining the fossæ nasales (Read). Lindenbaum relates two cases of tuberculous retropharyngeal abscess (see Northrup). Since tuberculosis of the palate and pharynx is far more frankly declared than that of the tonsils, it is much more frequently observed, but the number of cases permits, on this account, of no inferences as to the relative frequency of localization in these areas.

This is hardly the place in which to enter further into a discussion of the cases that have been reported since the original labors of Isambert and B. Fränkel. For the guidance of the reader, I refer him to the observations of Bucquoy, Krause, Conciliis, Dignat, Rey, Zawerthal, Finkler, Voltolini, Sevestre, Kasanski, Blois, Cutton, Malmsten, Hinkel, Wroblewski, fourteen cases of Hering, Lennox Browne, Palazzolo, Israi, Corradi, Zarniko, Griffin; further, for the cases of miliary tuberculosis of the pharynx, etc., B. Fränkel, Cadier, Löri, Rethi, Letulle, Catti, Küer, etc.

The lupoid form of pharyngeal tuberculosis, induced, as a rule, by extension from the external integument or the skin, has been described, among others, by A. Stockholm, Bull, Holmes, Cognacq, Bride, Downie, and Semon (in whose case dermal and nasal lupus were not present).

The rarity of tuberculosis of the oropharynx, which has indeed been entirely thrown out by some authors, has been already mentioned.

Since the assumption of a primary disease depends very largely upon the absence of demonstrable signs of disease in the other organs, especially in the lungs, *intra vitam*, we should be very guarded, in view of the imperfections of our methods of clinical research, in inferring the primary nature of the disease. Such cases, which within a few weeks or months develop a patent pulmonary tuberculosis, are not to be regarded as positive evidence, even though there is no doubt that primary oropharyngeal disease may be succeeded by a rapidly developing phthisis of the lung. Thus we cannot accept Isambert's famous case as definite proof of a primary pharyngeal affection. In this case a boy of four and one-half years presented tuberculous ulcerations of the velum, without any positive signs of pulmonary tuberculosis. He had, however, in early infancy given symptoms of scrofula and of scrofulous (?) coryza.

There is no possible exception to be taken to Fairlee Clarke's case as an example of primary disease. An eighteen-year old boy, without hereditary taint, developed extensive tuberculosis of the mouth, with almost complete destruction of the soft palate; the lungs were found normal, both clinically and post mortem.

Primary tuberculosis of the oropharynx seems most frequently to involve the region of the palate. Küssner, 1884, had four such cases. Kessler reports a primary palatopharyngeal tuberculosis from the ear clinic, and a primary tuberculosis of the tympanum. A thirty-five year old woman developed a tuberculous ulceration of the velum (tubercle bacilli histologically determined), which was cured by appropriate measures (Uckermann).

The tonsils, especially, play a rôle as primary situations. Abraham, 1885, demonstrated tonsillary tubercles in a scrofulous woman, in whom fauces, pharynx, larynx, and lungs were healthy. Lennox Browne described tuberculous ulcerations (tubercle bacilli) of the left tonsil in a woman with a healthy larynx and lung. Hopkins described a tuberculous ulcer of two years' duration upon the right tonsil, and a small one upon the inner surface of the right cheek, which extended over the upper and lower lip. Sacaze found in a young man of 22, with apparently healthy lungs, a tubercular inflammation of the tonsils (tubercle bacilli) without ulceration, and, simultaneously, a marked infiltration of the cervical glands, and general emaciation. Mention has already been made of the tubercles found by Orth and Krückmann in the tonsils of certain diphtheritic children. These cases are of especial importance, since in them the freedom of the other organs is clearly declared. Ruge observed in a strong girl of eighteen, hereditarily untainted and with otherwise healthy organs, an extensive tuberculosis of the right tonsil, which was succeeded by a myelitis of a part of the cervical segment.

Among the cases of tuberculosis of the anterior portion of the mouth, especially the tongue, there are a large number in which the other organs, notably the lungs, were found healthy at the time of the first examination. We may mention Fleming, Bonzenet (apical disease, eight months after the appearance of lingual ulcers), Bourcheix, Trelat (first thoracic signs ten months later), Laboulbene (apical signs only after fifteen months), Ponzerges, Isambert, Nedopil, Bryson Delavan, Wedenski, Paget, Gleitsmann, Crossfield.

Schlieferowitsch observed two cases of lingual tuberculosis which were free from disease of the lungs, and which remained so as long as kept under observation (Cases 2 and 11). The cases of Clifford Reale, Kaurin, and Wohlauer are not entirely unexceptionable, since the beginning of the pharyngeal disease was shortly followed by tuberculosis of the lung.

More convincing is Morel Lavallée's case of oral tuberculosis. The disease began in 1882 with laryngitis; four years later there was tuberculosis of the arches of the palate, and six years later callous ulcers upon the margin of the tongue at the pressure sites of the teeth. The lungs were sound as late as 1889.

Gleitsmann accomplished a cure in a case of primary tuberculosis of the mouth and pharynx. Pluder, also, recently recorded a case of primary pharyngeal disease.

A case of primary tuberculosis of the gums and of the mucous membrane of the cheeks, with large numbers of tubercle bacilli in the cavity of a wisdom tooth, has been described by Morelli. Stark, too, in a case of his, regards a carious tooth infected by tubercle bacilli as the portal of entry of the tuberculous virus. Scholz found a tuberculous ulcer upon the upper lip of a man of eighty-one, otherwise healthy, and von Eiselsberg has described an exactly similar case.

The lupoid form has been described as primary in several cases: once in the pharynx, by Schleicher; upon the uvula, the tonsils, and the anterior arches of the palate, by Moussous; upon the uvula and in the pharynx by Wright, and upon the palate by Treitel.

At times, chance injuries can be determined as the gateways of infection. A hospital orderly was scratched upon the upper lip by an insane man who also had lupus, and developed at the site of the injury a lupoid ulcer, which in two months spread over one-half of the upper lip (Plotnikow). A baker of sixty-three years, sound in his lungs and other organs, developed a tuberculous tumor of the size of a walnut upon his tongue, with swelling of the submaxillary glands, as a result of burning his tongue with a cigar (Graser). Grawitz saw tuberculosis associated with a carious molar in a healthy, untainted fusileer; the first sign was swelling and caseation of the corresponding cervical glands, followed in six months by pulmonary tuberculosis. A cannoneer fell sick of a tonsillitis with a diphtheritic membrane, from which proceeded a tuberculous infection of the cervical glands with subsequent general miliary tuberculosis.

It would be contrary to actual facts if, in the face of these clinical contributions to the etiology, we should be doubtful as to the primality of the affection, and should postulate a hematogenous origin, derivable from some focus inherited from parents or grandparents, remaining latent and unsuspected in the body.

Even in secondary tuberculosis of the oropharynx, which is regarded by Voltolini, Abercrombie, and Gay simply as part and parcel of a general miliary tuberculosis, there are certain facts which declare against a hematogenous origin, and in favor of an infection by the sputum. Thus it occurs, as a rule, in mature individuals with consumption, who expectorate their sputum; while in children, who swallow their sputum, it is only rarely found, notwithstanding the increased tendency in early life to hematogenous infection. The conditions for such infection are most favorable in general miliary tuberculosis produced by a flooding of the blood-channels with bacilli.

Not rarely, oropharyngeal disease may be derived from neighboring tuberculous or lupoid foci in the nose, external skin, or larynx, arising by continuous extension, by contact, or by lymphoid transmission. In the same fashion an oropharyngeal focus advances, being aided materially in this by the tongue, which touches alternately the healthy and the diseased areas.

Markedly frequent in connection with oropharyngeal disease, and generally dependent upon it, is swelling of the cervical glands, which will be treated of later as one of the most characteristic signs of scrofula.

[Koplik* reports an apparently primary case of tuberculosis of the tonsil, in which the disease was ascribed to a definite exposure to infection. He describes a second case, in which enlarged and cheesy cervical lymph-nodes were ascribed to a primary tuberculosis of the tonsil. He then describes a third case of even greater interest, in which a child died of acute general miliary tuberculosis, and in which the only old cheesy foci found were in the tonsils, so that it was concluded that the starting-point for the general infection was the tonsillar disease.—Ed.]

Infection of the Esophagus.—In the esophagus tuberculous processes are even more rarely met with than in the oropharynx. Its well-developed layer of squamous epithelium, of which the capacity for resistance has so often been demonstrated (I need only mention the glass and stone eaters, and the sword swallowers), provides an effective external defense. Food and sputum, enclosed in slippery mucus and saliva, slide rapidly through the esophageal tube, and are thoroughly mixed by the constrictor muscles. Slight remnants are washed along by fluids swallowed, so that the arrest of bacilli by the mucosa is almost impossible. So far as I am aware, a primary esophageal tuberculosis has not yet been described. Even in consumptives, who swallow large quantities of their sputum, disease of the esophagus occurs but rarely, and the same holds true of animals.

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* Amer. Jour. Med. Sci., Nov., 1903.

The earlier observations of Oppolzer, Pauliki, Chvostek, Kraus, and Zenker are partly incomplete, lacking histological confirmation. Except a short notice of Orth's that he had found tubercle bacilli in esophageal foci, the earliest positive observations date from Breus, Eppinger, Weichselbaum, and Beck. Recently Cone gave a summary of the 48 cases of esophageal tuberculosis hitherto recorded.

Infection of the esophagus occurs most easily from its exterior surface where the defensive action of its epithelium is lost; the attack of the enemy, in other words, is from the rear. Caseous and suppurating bronchial and tracheal glands, which lie in contact with the wall of the esophagus, are especially apt to become adherent by inflammatory processes, and to break through into the lumen of the canal.

A rupture of this nature is more often the cause of esophageal tuberculosis than is the swallowing of sputa. For, in the first place, the virus, which forces its way in from the exterior, is enabled to advance stealthily along the lymph-channels beneath the epithelium; and, secondly, after the first perforation, small particles only find their way successively into the esophagus, in which they fail to excite a contraction, remain at rest for a time (Weichselbaum), and, by virtue of the absence of an envelope of mucus and saliva, come into far closer contact with the mucosa than do sputa. A case of this character is described by Weichselbaum. In the autopsy of an individual of thirty-six years, he found extensive caseation of the cervical and mediastinal glands, and multiple perforations of the posterior wall of the trachea and of the anterior wall of the esophagus, which were in communication with the suppurating glands which lay between them. The mucous membrane of the esophagus and of the trachea above, but more especially below, the site of perforation was covered with numerous tubercles and in part ulcerated. The lungs were only slightly affected, and the foci were almost entirely confined to the larger bronchi. The ileum presented a few caseous solitary follicles.

Beck describes a similar autopsy finding in a man forty-five years of age, in whom there was a tuberculous ulcer of the esophagus between the upper and middle thirds; it was caused by the perforation of a tuberculous gland, and encircling it were numbers of small, partially disorganized nodules.

In Selenkow's case a man fifty years old complained of severe pain under the sternum, which was increased by swallowing and presented the symptoms of stenosis of the esophagus; here the substance of the esophagus was found to have been replaced over a space of 4 cm. by a caseous glandular or pulmonary focus.

Zenker observed a woman forty-six years of age, cachectic, with operated cervical glands, small pulmonary cavities, and tuberculous pleurisy, who at the same time presented a perforation of the esophagus produced by caseous gland, with an extension of the process into the mucous and muscular layers, and with three tuberculous ulcers in the gut. Since the development of such esophageal tubercles following upon a perforation requires considerable time,—at least a number of weeks,—it is, as a rule, absent in cases in which death occurs soon after the perforation.

Such perforations, unaccompanied by actual esophageal foci, are mentioned by A. Neumann, Poland (in a child one and one-half years old, perforation into left bronchus and esophagus), Barry (man of seventy-one years, sudden death by pulmonary hemorrhage, gland fistula leading to esophagus, trachea, and vena cava superior), Hanot (man twenty-two years old, perforation into esophagus and trachea, "de petites nodosités grisâtres," taken for closed follicles, in the lower portion of the esophagus), Nowak (in a woman of sixty-one years, primary tuberculosis of bronchial glands with rupture into esophagus, pericardium, and trachea, subsequently miliary tuberculosis), Völker (in a boy of seven years, perforation into the esophagus, no symptoms), and by Penrose.

In other cases such glandular perforations may heal up without the further development of tubercles, and may give rise now and then to traction diverticula. At times there is not even perforation, but only a more or less pronounced grade of stenosis. A case reported by Glockner is also referable to the glands. In a forty-seven-year old consumptive, with caseous peribronchial lymph-nodes, he found a circular zone of caseous nodules in the esophagus, especially in its muscular coat, and a number of string-like whitish strands with miliary nodules running to the lymph-nodes; the latter were caseous 3 cm. above the esophageal focus.

In the same way infection of the esophagus is apt to occur when the surface is locally denuded of its epithelium. At the autopsy of a consumptive who had attempted suicide by drinking caustic potash, Breus found numbers of tuberculous ulcers in the pharynx, esophagus, and stomach, in addition to the stenotic cicatrices. There was also tuberculosis of the lungs, of the large and small gut, and of the corresponding glands, and, finally, recent tubercles in the liver, spleen, and kidneys. In a woman of forty-five years with chronic ulcerative pulmonary tuberculosis, Eppinger observed an almost occlusive growth of mould throughout the entire esophagus. After carefully washing away these masses, he discovered that the mucous membrane all the way from the cardia was beset with tubercular ulcers and miliary tubercles. Kundrat observed esophageal tuberculosis as a sequel to the corrosive action of sulphuric acid. Zemann also records a similar condition resulting from chemical destruction of the mucosa.

Epithelial defects are at the bottom of the formation of tubercles upon a carcinoma of the esophagus. Miliary tubercles upon the base of a cancerous growth of the esophagus have been described by Zenker and by Cordua—by the latter in case of a man of sixty years, with a rapid, ulcerative pulmonary phthisis. The contention of Cordua's that the case was one of lymphogenic infection, I cannot admit; first, because the small particle which was submitted to examination and which showed more tubercles in the depth of the tissue than at its surface cannot be taken as a criterion of the entire tumor; and, second, because the theory of sputal infection is *à priori* far more reasonable. The opposite process of metamorphosis of an esophageal ulcer into a carcinoma has been observed by Pepper and Edsall.

A thirty-eight year old consumptive, observed by Bauer (Nürnberg) and Zenker, with pronounced dysphagia, presented cavities in the lungs, and, in the uppermost portion of the constricted esophagus, a cicatrized, tuberculous ulcer, embracing the entire circumference of the canal; the bifurcation glands were permeated by tubercular foci; the gut was free.

In some cases tuberculosis of the esophagus has been observed even in the absence of favoring circumstances. Mazzotti had two cases of consumption, a man of thirty-nine and a woman of thirty-seven years, in which tuberculosis of the esophagus was associated with ulcerations of the gut. The less actively sputum is driven into the stomach by the food and drink the more pronounced becomes its caustic actions. The epithelial denudation, which Mazzotti found in a consumptive who was in the habit of swallowing the profuse secretion from his cavity, may perhaps be regarded as the first stage of the process.

The process may also advance subepithelially from the pharynx and larynx, the epithelium being undermined and lifted off, as could be very plainly followed in a case of Beck's. A fifty-four-year old consumptive had, in addition to tuberculosis of various organs, miliary tubercles in the liver, spleen, and kidneys, and an extensive ulcerative process in the larynx and epiglottis, which involved the pharynx and the upper esophagus, embracing the entire circumference of the latter. Gray miliary tubercles were discernible through the intact epithelium for some distance down, gradually getting fewer in number; evidently these originated by extension of the bacilli along the tissue spaces.

A similar mode of origin, that is, by continuous extension, was accidentally observed by Zenker in a youthful consumptive. In addition to tuberculosis of the lungs, trachea, and larynx, the esophagus at the level of the bifurcation presented a tuberculous focus of the size of a 25-cent piece, while the submucosa and the muscularis were riddled with caseous nodules, and, almost completely adherent to the diseased area of the esophagus, was a caseous bunch of lymph-glands.

Finally, Mazzotti observed tuberculosis of the esophagus without ulceration in a boy of ten years, who had developed a general acute miliary process on top of a caseating bronchial gland. The case does not permit of the exclusion of a hematogenous origin, but is just as probably an example of direct extension from the glands.

Infection of the Stomach.—Tuberculosis of the stomach, as of the esophagus, is one of the rare varieties of the disease. In 1895 Letorey was able to collect in all 21 cases in the literature, and asserts that their specific nature is macroscopically revealed only by small nodules in the diseased area and around it. As a primary condition, independently of tuberculosis of other organs, it has never been found.

The same factors which render an infection of the esophagus difficult act similiarly in the stomach. It is true that the ingesta remain in the stomach far longer; but, on the other hand, the acid reaction of the gastric juice acts as an additional impediment to the growth of the bacteria. Here one may truly speak of a poor medium, of a diminished predisposition, which is betrayed, even in the few cases of tuberculous gastritis recorded, by the small number of bacteria found. Certain authors, especially Wesener, have conducted experiments which led them to maintain that the succus gastricus is capable of destroying the tubercular virus. The researches of Frank and Fischer have, however, a different tenor. Zagari, also, showed that tubercle bacilli could travel through the entire intestinal tract of the dog and still not lose their virulence. Exposure of tubercle bacilli to the gastric juice of the dog for a period of time corresponding to that ordinarily consumed in digestion, two to three hours, was insufficient to destroy them; eighteen to twenty-four hours were necessary. Straus and Wurtz reached a similar result with pure cultures of avian tuberculosis. Cadéac and Bournay removed tubercle bacilli from the stomach of a dog fed with tuberculous material and demonstrated by inoculations that they were still virulent.

Granted that the bacilli do not perish in the stomach, it nevertheless holds true that the normal, and even pathological, gastric juice but very exceptionally permits tubercle bacilli to settle and multiply in the stomach wall. Even in chronic phthisis, in which there is an extreme reduction of free HCl, the probable bactericidal agent, and in which extensive intestinal ulcers indicate the possibility of infection by the swallowed sputum, such specific lesions are only rarely found.

Barbacci believes that in the stomach, as in the gut, the lymph-follicles constitute the primary seat of the disease, and that their comparative rarity in itself presupposes the infrequency of gastric tuberculosis.

In a case of this character, described by the same author, a young soldier presented a severe pulmonary tuberculosis and tubercles disseminated over almost the entire small intestine; in the stomach were four large tuberculous ulcers, of which one encircled the pylorus, and, in addition, a number of caseous glands at the lesser curvature.

One would expect, and indeed Klebs asserts this, that tubercle bacilli would easily gain a footing in circular gastric ulcers, which are especially frequent in anemic and chlorotic persons and which are ascribed to a diminution of the alkalescence of the blood with a simultaneous hyperacidity of the gastric juice. Statistics upon the frequency of coincidence of these two phenomena are, however, widely at variance. Musser flatly denies the occurrence in cases of preëxisting phthisis. According to Hérard, Cornil and Hanot, who refer to Dietrich, Cazit, Steiner, and Volkmann, the ulcus rotundum is in 22 per cent. of the cases accompanied by tuberculosis. Sokolowski saw at autopsy a gastric ulcer which perfectly imitated an ulcus rotundum, and in the base of which numerous tubercle bacilli were discovered. Litten found a tuberculous ulcer in the stomach, without there being any other demonstrable tuberculous changes in the intestinal tract.

Przewoski, who found tuberculous gastric ulcers in five autopsies, associates them with the extremely chronic fibroid form of pulmonary tuberculosis in which bacilli are carried to the stomach over a long period of time. He invariably found an accompanying catarrhal process.

It is the rule that gastric tuberculoses caused in this way by the swallowing of sputa are combined with extensive specific alterations in the gut, which is similarly exposed and at the same time more strongly predisposed to infection. The latter may nevertheless be absent when the infection has followed other channels. As such, we must especially consider tuberculous lymph-nodes upon the lesser curvature, which may draw the gastric wall into a sympathetic disturbance *a tergo*. Chiari has described a perforation by tuberculous lymph-glands.

The infection may also be originated by invasion from the peritoneum. Birch-Hirschfeld describes two such cases. In a man of forty-seven years who had suffered severely from gastralgia, Hattute found pyloric stricture occasioned by numerous partially ulcerated tubercular nodules with a consequent gastrectasia, associated with a diffuse peritoneal tuberculosis. Finally there are cases to which a hematogenous origin may be ascribed.

Eppinger contributes two such observations. In a case of old pulmonary tuberculosis and recent miliary tuberculosis in the liver, kidneys, and spleen, he found the condition which he considers characteristic of hematogenous disease, namely, large numbers of tuberculous ulcers, of various size, distributed over the entire surface of the gastric mucosa, numerous miliary tubercles, and at the same time an unaffected intestinal canal.

Here, too, belongs a case of Mathieu's, of a man of fifty-eight years with miliary tuberculosis of the lungs and tuberculous ulceration of the stomach; and an observation of Cazin's, of an extensive round ulcer, with irregular, tuberculous margins, situated upon the posterior wall of the stomach in a girl of twelve years, who also had suppurative lymphadenitis colli and pulmonary tuberculosis. In the latter case there was frequent hematemesis.

According to Musser, children present gastric tuberculosis more frequently than adults. Kaufmann found it only in children with severe miliary tuberculosis. This fact is perhaps partially attributable to the diminished digestive power of children, in part to the increased disposition of that age to miliary tuberculosis in general.

[Van Wort* reports a unique case of solitary tubercle of the stomach situated in the muscularis. It was impossible to determine whether or not the lesion was primary in the stomach.—Ed.]

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* Johns Hopkins Hosp. Bull., Sept., 1903.

Infection of the Intestine.—The relative rarity of tuberculous disease in the upper portion of the digestive tract is in marked contrast to its frequency in the intestines. Intestinal tuberculosis appears under the form of isolated or multiple nodules, situated in the mucous membrane, which either calcify or become converted into ulcers which circularly embrace the gut.

In certain rare cases, one of which is described by Grawitz, the caseous nodules distributed along the gut attain the size of peas or beans, lie in the submucous tissue, produce localized prominences of both mucosa and serosa, and then give rise to ulcers with overhanging edges, and to defects involving the entire tissue down to the peritoneum, corresponding to the necrotic, caseous plug which is extruded.

The circular disposition of the tuberculous intestinal ulcers, which is contrasted with the longitudinal axis of typhoid ulcers, is ordinarily attributed to the invasion of the arteries of the gut by the bacilli. This explanation is hardly sufficient, since the vessels proximal to the tubercles are as a rule obliterated. It is more probable that the localization and dissemination of the bacilli derived from the disorganized tubercles follow the course of the circular lymph-spaces, and are here furthered by the circular muscle-fibers. The intestinal ulcers meet with a certain degree of resistance in eating their way through the muscularis, but, if they overcome this, are capable of perforating through the serosa into the peritoneum or into adherent viscera. Kaufmann observed perforation of a tuberculous intestinal ulcer into a myomatous uterus.

Occasionally intestinal ulcers go on to recovery, as is evidenced by the scars which are frequently found at autopsy in association with recent foci of disease. The cure of large girdle-ulcers may be complicated by stricture of the gut. This event is not so very rare an occurrence—König observed five such cases within two years—and sometimes these may become the occasion of brilliant surgical interference.

The follicles are the first seat of miliary tubercles in the gut. Virchow regards the wealth of follicles of the intestinal mucosa as directly responsible for the access of tuberculosis.

Hanau was in so far able to confirm this, that of three consumptives with cavity formation, he found one who showed no Peyer's patches to be absolutely free from intestinal tuberculosis; while in the other two, corresponding to the low grade of development of the follicles, the gut was involved only to an insignificant extent. In animal experimentation also the first changes are apparent in the follicular apparatus (Baumgarten). The cause of this phenomenon is not to be sought in a special predisposition, a diminished power of resistance, of the follicles, but is referable to the fact that they are organs of absorption, and as such take up also indifferent matters mingled with the food, carmine, pigments, etc., with similar alacrity (Kleimann). Thus we get at least a partial explanation of the fact that tuberculous processes in the gut prefer the areas well supplied with follicles, the lower part of the ileum, ileocecal valve, and the appendix, the mucosa of which is often metamorphosed to a caseopurulent plug (Rokitansky, Bierhoff, Baumgarten).

Höning asserted that in closed, non-ulcerative follicles neither tubercles nor giant cells nor bacilli were to be found, and that tuberculous ulceration of the gut was therefore possibly a sequel to a preceding non-tuberculous ulceration. This theory, which is a pendant to Dettweiler's and Meissen's hypothesis of pulmonary tuberculosis, has been amply discredited by the thorough researches of Herxheimer and others.

As a rule, distribution of the bacilli takes place from the wall of the gut to the corresponding mesenteric glands, which often swell up and form large masses. Occasionally the glands are scarcely altered in volume, but reveal small caseous foci or points. This tuberculosis of the mesenteric glands sometimes occurs without demonstrable changes in the wall of the gut. In other words, the bacillus has the power to penetrate not only the intact epithelium (Baumgarten, Dobroklonski, and Tschistowitsch), but also the entire wall of the gut, and to find its way along the lymph-channels to the mesenteric glands, where it first begins its actual career (Orth, Wesener, and the author). This it accomplishes partly by mechanical means, partly by the aid of the wandering cells, and all without leaving behind a recognizable trace of its passage.

Baumgarten disputes the fact that the bacilli pass through the wall of the gut without any attempt to remain and develop. Since, however, he admits that at least a certain number of the bacilli find their way direct to the mesenteric glands, it is hard to understand why this should not hold true also for the remainder, or, indeed, for the whole number of bacilli where few are involved. For the rest, Baumgarten's contention is opposed by the conditions at some of the autopsies of children, in which there is a mesenteric tuberculosis without any changes in the gut; further, the findings in animals after feeding experiments of sufficient duration, and the analogous condition in the respiratory tract and the other mucous membranes (Cornet), tend to discredit this view.

Glandular tuberculosis of the mesentery without any disease of the gut itself, which is etiologically equivalent to intestinal tuberculosis, plays a prominent rôle in the diseases of childhood. Tabes mesaraica, as it is called, depends largely upon the heightened permeability of the infantile skin, mucous membrane, and lymph-vessels, a condition which also finds expression in the frequency of tuberculosis of the cervical and bronchial glands, in the absence of all disease of the main avenue itself. In the glands an imperative halt is called to the progress of the bacilli. According to all previous observations, further advance to the ductus thoracicus and the blood-channels is possible only when the glands have been deprived of their "filtering" power by tissue changes gross enough to be actually seen.

[Macfadyen and MacConkey* took mesenteric glands from the bodies of children who had died of other diseases than tuberculosis, and who, at autopsy, were found to be non-tuberculous, and injected material from these glands into guinea-pigs. In 25 per cent. of these cases they obtained evidences of tuberculosis. From this they conclude that virulent tubercle bacilli are present in the mesenteric lymph-nodes of children more often than had been supposed, and that the intestine is more important as a port of entry for tuberculosis than the tonsils and adenoids.—Ed.]

Tubercle germs may be carried into the gut along with accidentally infected food, or by being deposited from the respiratory air in the mouth or nose and then being swallowed. Far more frequently, however, infection is due to the use of the flesh and milk of tuberculous animals. This is not the place to give even a brief summary of the numerous researches which, from the time of Chauveau and of Gerlach, have repeatedly demonstrated the danger of such food. This conclusion depends not only upon inoculation and feeding experiments, but also upon the demonstration of the tubercle bacilli in the food.

[Nicolas and Descos† fed to dogs soup to which tubercle bacilli had been added, and subsequently found tubercle bacilli in chyle from the thoracic duct. They claim to prove in this way that the bacilli can pass through the uninjured intestinal mucous membrane.—Ed.]

I refer among others to Virchow, Biedert, Toussaint, Wesener,

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* Brit. Med. Jour., July 8, 1903.

† Jour. de phys. et path. gen., 1902, iv, 910.

Eggers, de Maurans, Nocard, Bollinger, v. Chlapowski, Macfadyen, Kastner, the "Sächsische Bericht,"—Bang, Galtier, Robcis, Legru, Crookshank, Niven, Hirschberger, Heller, Ernst, Burdon, Heim, Gasparini, Roth,—Nocard and Bollinger.

The final result may thus be summarized: The flesh of tuberculous animals is regularly to be regarded as infectious in severe types of the disease; in milder forms of the disease, when it is still fairly well localized, infectiousness is rather the exception. The same holds true of milk and its products, butter and cheese (Heim, Roth, etc.), only that here local disease of the udder is a further source of infection.

The disquieting assertions of some authors, to the effect that the ordinary market butter in 47 per cent. (Gröning) or even 100 per cent. (Obermüller) of the specimens contains virulent tubercle bacilli, have been fortunately overthrown. According to the investigations of Petri and Rabinowitsch, these erroneous conclusions depend in part on a confusion of the butter bacillus with the morphologically similar tubercle bacillus.

The danger of an infection through meat is largely diminished by the fact that not all the diseased animals, but only those very severely affected, act as a source of infection. A well-regulated supervision of the slaughter-houses secures the rejection not only of the actually affected areas but also of all the flesh of animals seriously diseased; and the method of preparing the meat of cows, the animals most in question, appreciably lessens the possibilities of infection, since the temperature of boiling water may be relied upon to destroy the virulence of the tuberculous poison.

And yet sufficient opportunities for the invasion of the gut by bacilli are furnished, first, by the inadequacy of meat inspection; second, by the preference of some individuals for preserved or smoked meat, which loses none of its infectiousness through these processes (Förster); and, third, by the greed of certain sausage-makers who make use of directly diseased meats. Far more dangerous in this connection are the milk and its products, since their source is almost incapable of accurate supervision. In addition, they are used in large quantities, and, because of their flavor and easier digestibility, for the most part uncooked or only slightly warmed.

Certain authors have attempted to vindicate the harmlessness of these foods. So Schottelius records that in Würzburg an experimental investigation was made of the consequences resulting from the use of tuberculous flesh. Of those who employed this meat in the suburbs of the city, and who were under the direct supervision of the district physicians, not a single individual developed the disease, although the meat was eaten in every form—boiled (!), broiled (!), as sausage, and even raw. Gallaverdin records that he and his family and his patients had for years drunk the uncooked milk of a cow whose viscera were found at slaughter to be richly studded with tubercles, and yet they had suffered no injury therefrom. Such communications are not to be weighed against the innumerable contradictory experiments and clinical records, although individually they may indeed be difficult to explain.

Clinically, infection by tuberculous food is indicated when tuberculosis of the gut occurs as a primary infection, especially when the pathological conditions coincide. Buhl makes mention of the case of a five-year old boy without tuberculous antecedents who died of tuberculosis of the internal organs following the continued use of tuberculous milk.

Demme, who has won special distinction through his careful sifting of such cases, describes the case of a child of healthy family who died of extensive intestinal and mesenteric tuberculosis, the meninges and lungs being sound. The infection was attributed to the use of milk coming from a cow which died eight weeks later of tuberculosis. Further, he demonstrated intestinal tuberculosis in four untainted children, following upon the use of raw milk from a tuberculous cow. Within one year Demme observed seven cases of primary tuberculosis of the gut and mesenteric glands, limited to these organs. He described also the case of a four-months old infant, without hereditary taint, who presented isolated disease of the mesenteric glands; the child had been brought up on the raw milk of a cow which was found at slaughter to be tuberculous.

According to another observation of the same author, four hereditarily untainted children died within a short time of primary isolated intestinal tuberculosis (autopsy). The infection was traced to the following circumstance: The nurse of these children had the habit of trying the heat of the spoon with her lips before feeding porridge to them. Two months after the death of the fourth child it was discovered that this nurse had a lupus of two years' standing upon the inferior portion of the nasal septum, and also tuberculosis of the antrum of Highmore, from which tuberculous pus was voided through a fistula into the mouth.

Ollivier writes of a boarding-school in which thirteen girls sickened and six died of tuberculosis, and in several of these the disease was primary in the gut. The milk consumed in the school was derived, as was afterward ascertained, from a tuberculous cow presenting pronounced lesions of the udder.

Another case with anatomical authentication is furnished by Wyss. A five-year old girl who died of diphtheria had a nodule of the size of a millet-seed in the small intestine, and a caseous mesenteric gland containing tubercle bacilli. It was shown that the child had for some time drunk uncooked milk. A man of 31 years, who, according to his own statement, had lived for seven years upon eggs and raw meat exclusively, presented post mortem three intestinal ulcers, caseous mesenteric glands, and a fresh, caseous consolidation of the lung with a focus of softening of the size of a pea; otherwise there were no tuberculous changes, the bronchial glands being intact (Behrens). Schlenker found tuberculous intestinal ulcers in a boy of six years, with tuberculosis of the diaphragm, of the mesenteric, thoracic, and cervical glands, and of the tonsils, and scattered submiliary tubercles in the spleen, kidneys, and lungs. Analogous cases are recorded by Epstein, Baginsky, Herterich, Hermsdorf, and Eisenhart.

The extraordinary difficulty of demonstrating the source of such infection has already been pointed out, for very few individuals are aware of the source of their food, *e. g.*, dairy milk. How is one to demonstrate the origin of the food or the condition of the animals to be suspected, weeks and months after such an infection has taken place, when the earliest clinical symptoms make their appearance?

One will hardly err in adding to the list of food infections the numerous cases of isolated or predominant mesenteric tuberculosis in infants. In addition to the increased permeability of the child's mucous membrane above mentioned, the almost exclusive milk diet, often amounting to one-seventh of the body-weight, contributes to the frequency of intestinal infection in the earlier years.

Great as is the importance of intestinal infections, it is certainly going too far to assert, as does Klebs, that the gut is the chief avenue of infection in most cases of tuberculous disease. For even in childhood intestinal infection, which is then far more frequent that in later life, is completely overshadowed by primary infection of the respiratory tract. If one makes a comparison of the two groups of organs on a basis of the condition of the corresponding lymph apparatus, which in childhood constitutes the chief expression of the disease, one finds that tuberculosis of the bronchial glands is far more frequent than that of the mesenteric chain.

Biedert collected the autopsy findings in tuberculous children from the reports of Simmonds, Rilliet and Barthez, Steiner and Neureutter, Widerhofer, and Steffen, and others, and presented the statistics as follows: In 1346 cases, the disease was localized in the lungs, 79.6 per cent.; in the bronchial glands, 78 per cent.; in the gut, 31.6 per cent.; in the mesenteric glands alone, 40 per cent.

According to Carr, in 120 autopsies of tuberculous children the lungs were caseous in 90, or 75 per cent.; the bronchial glands in 96, or 80 per cent.; the gut in 66, or 55 per cent.; and the mesenteric glands in 65, or 54 per cent. The latter were the sole seat of disease in only five of the cases; in the other 60 cases the thoracic glands were also affected, and indeed in a very pronounced degree. After our determination of the laws governing the localization of the tubercle bacilli, we are hardly called upon to show in further detail that cases in which the only, or the principal, changes occur in the lung cannot be attributed to intestinal infection.

In contrast to the primary cases of intestinal infection, occasioned chiefly by the food, are the innumerable cases of secondary disease, such as originate in connection with pulmonary phthisis. They are so frequent that one may almost regard them as the customary accompaniment of chronic pulmonary tuberculosis, even though in life they may give rise to but few active symptoms.

Eichhorst in 462 autopsies on cases of pulmonary phthisis found intestinal ulcers in 29.9 per cent.; Heinze, in 1226 cases of consumption, 51 per cent. of tuberculous disease of the gut; Höning in 70 per cent.; according to other authors, they occur in 90 per cent. (Weigert, Orth); Baumgarten found them rarely absent; Herxheimer observed them in 57 out of 58 cases of phthisis.

The cause of this frequent coincidence of the two diseases depends primarily not upon an increased predisposition of the intestinal mucosa, but on the opportunity afforded of carrying large quantities of tubercle bacilli into the gut by the constant swallowing of tuberculous sputum. Thus it is that tuberculous cases in which the lung is not affected—and, consequently, the above-mentioned predisposing factor is excluded—show tubercular changes in the gut far less frequently. For the same reason, extensive experimental tuberculosis in animals is, as a rule, not accompanied by disease of the gut, because it does not proceed, as in human beings, with cavity formation and profuse secretion.

In my experiments with over 3000 animals, excluding the feeding experiments, tuberculous foci in the gut and in isolated mesenteric glands were found hardly more than six to eight times, in spite of the most extensive disease of the other organs (so-called "marked predisposition"). Even these few cases are possibly to be explained as due to the licking off of external tuberculous areas, or to the accidental admixture of tuberculous products with the food.

Even before the discovery of the tubercle bacillus, Klebs connected the tuberculosis of the gut in phthisis with the swallowing of sputum. Mosler especially emphasized this danger, after he had found extensive tuberculosis of the jejunum and the ileum in a patient obstinately addicted to swallowing his infected sputum. Sauerhering brought a further confirmation of this theory by recording the frequency of symptoms of intestinal tuberculosis in idiots, who are in the habit of swallowing their sputum, as seen by him in his institution for imbeciles and the weak-minded. The etiological relation between the swallowing of sputum and the origin of intestinal ulcers is also revealed by the fact that in acute as in chronic miliary tuberculosis such ulcers are missing unless there is cavity formation.

Intestinal infection is also produced by the rupture of a caseous bronchial or mediastinal gland into the esophagus. The question which now confronts us, as to whether the use of infected food or the swallowing of tuberculous sputum is invariably followed by ulceration of the gut, must be positively answered in the negative. Not alone the previously detailed statistics but also theoretical considerations point this to be the case. There are, indeed, certain peculiar conditions in the gut which serve to render its infection difficult. In the first place, all ingesta are retained for only a brief period, for a few hours, in the gut; consequently foreign bacteria are unable to multiply appreciably unless they proliferate with extreme rapidity, as do the cholera and the typhus bacilli. An increase of tubercle bacilli in the gut is an *à priori* impossibility, the more so as they are outclassed in the struggle for existence by other bacteria.

The acidity of the gastric juice seems to impair the vitality and the proliferative energy of the tubercle bacilli temporarily at least, though it is again offset by the alkalinity of the intestinal juices. The rapidity of their passage, added to the protection afforded to the epithelium by the mucous secretion of the glands, renders it difficult for the bacteria to attack or invade the mucous membrane. Such as do gain a footing are liable to be washed or brushed away again by the aftercoming particles of food.

Prolonged sojourn in one place favors infection. This is a further cause, in addition to the rich supply of follicles, why the cecum and vermiform process should be the favorite seats of tuberculous as of other acute and chronic inflammatory processes. These two parts of the gut are especially liable to stagnation of contents and to erosions of the mucous membrane.

In the lower part of the rectum especially there is frequently a prolonged stagnation, with inspissation and hardening of the feces. The tough particles are then apt to excite excoriations into which the bacilli present in the feces force an entrance. Thanks to the extraordinary absorptive capacity and to the metabolic activity of this part of the gut, the organisms then stand an excellent chance of being carried well into the deeper tissues.

The frequent combination of anal fistulæ and of phthisis was recognized long before a suspicion of infection was entertained. Hippocrates had observed it (Cluron). The character of these fistulæ was first established by the demonstration of bacilli, by Lachmann and Smith. According to some authors, 5 per cent. of consumptives have rectal fistulæ; according to Hartmann, of 626 consumptives, 31, or 4.9 per cent., were so afflicted—of 447 men, 6 per cent., of 179 women, 3.35 per cent.

From the opposite point of view, Hartmann *(loc. cit.)* found that of 48 cases operated for rectal fistulæ, 23 were positively tuberculous, two were undetermined. The site of invasion often remains hidden, either because the excoriations have already become healed or because the bacillus has actually found its way through an uninjured mucosa—a feat the possibility of which has been sufficiently demonstrated.

Lesions of the mucosa facilitate the invasion of bacilli, hence their association with typhoidal ulcers. Whether simple catarrhs, without ulceration, also favor infection is doubtful. It may, on the contrary, be the case that the increase of secretion and swelling of the mucosa oppose a further barrier to the entrance of the tubercle bacilli. At any rate, the mucous membrane of rabbits when in a state of catarrhal inflammation refused to absorb india-ink, whereas the normal mucosa absorbed it readily (Kleimann). The experiments in infection of healthy animals in general, and the histological evidence of the existence of bacillary foci underneath normal mucous membrane in particular, would seem to indicate that epithelial lesions are not necessarily forerunners of infection. The development of an intestinal infection depends essentially upon the number of bacilli introduced.

Slight as is the possibility that isolated particles of india-ink mingled with the food will be taken up by the mucous membrane of the gut, just so slight is the same possibility for a few chance bacteria. Thus it is that in infections from milk and meat the lesions are sparse because the bacilli are few, while in infection from sputum the foci are generally numerous.

We have up to this point considered intestinal tuberculosis as an infection proceeding from the surface of the mucous membrane. Far less important is hematogenous infection, as a partial manifestation of general miliary tuberculosis. In this case it is the subserous connective tissue which is especially implicated (Tschernikoff).

In conclusion, we must still consider tuberculous ulcerations at the anus, which in the vast majority of cases are also due to an infection by means of feces. This affection is rare, thanks to the thick layer of epithelial cells, which often afford an efficient protection even against the extraordinarily filthy habits of some consumptives. One patient, a consumptive, told me that he suffered from a most obstinate constipation, which he could only overcome by forcibly extracting the feces with his fingers, the latter being moistened with saliva. Marianelli describes a similar case in a consumptive; Hartmann has added twelve new cases, including two original observations, to the previous collection of seventeen cases.

Kramer observed an ulcerated tumor of the size of a walnut in the anal region. Doutrelepont saw a lupus papillaris at the anus in two cases, in one extending over the buttocks. Occasionally the verrucous form of tuberculosis occurs. Riehl and Pick describe fibromatous tumors which they considered tuberculous. I have already made mention of the occurrence of lupus on top of tuberculous fistulæ and scars; such a condition was seen by Liebrecht in connection with the rectal fistula.

[For several years occasional cases of tuberculosis of the intestine have been noted in which there is a marked thickening of the wall of the gut. These have been called by the French "*Tuberculose intestinale, a forme hypertrophique*"; or, better, in English, "hyperplastic tuberculosis." The essential feature of the condition is a connective-tissue hyperplasia, brought about by an infection with the tubercle bacillus. The organism, in these cases, appears to encourage a new growth of connective tissue rather than cheesy degeneration, thus giving rise to a condition resembling hyperplastic tubercular processes in the serous membranes. The reason for the changed reaction is not known. As it usually affects the neighborhood of the cecum and vermiform appendix and forms a discoverable tumor during life, it is naturally often mistaken for cancer of these structures. Indeed, there is reason to believe that some of the cases of cancer of the cecum reported cured by operation were cases of this form of tuberculosis. When the disease is situated in the rectum, it may be confounded with syphilis. Lartigau[*] reports a case in which the above lesion affected the lower third of the ileum, the cecum, and the upper part of the colon. Crowder[†] reports a case in which the disease was limited to the vermiform appendix and adjacent portion of the cecum and which was cured by removal at operation. He concludes that secondary tuberculosis of the vermiform appendix is common, that primary tuberculosis of the organ is rare, but that the appendix is apt to participate in the hyperplastic change if this affects the neighboring parts.—Ed.]

INFECTION OF THE RESPIRATORY TRACT AND OF THE EAR.

Diseases of the lung are the most important of the tuberculous affections of human beings. For a long time their etiology was not understood owing to their supposed immunity from external influences. The theory that the air of respiration afforded a means of continuous and intimate communication with the external world gave the first real insight into the manner of infection. An actual demonstration of this etiological relationship was first furnished by Tappeiner, who succeeded in producing a typical pulmonary tuberculosis in dogs by forcing them to breathe the pulverized sputum of consumptives. The discovery of the tubercle bacillus, and the demonstration of this organism in the sputum, in air, and in dust, in combination with numerous animal experiments, permit of no doubt of infection through respiration.

Not all parts of the respiratory tract are exposed in equal degree to such infection. A few general observations will make this clear. If air is sucked up through a smooth tube, of equal bore throughout, the interior of which has been coated with a layer of gelatin, the bacteria contained in the air will find an unequal distribution in the gelatin, as shown by Hesse. They tend especially to be deposited toward the free extremity of the tube, and their number diminishes progressively with the distance from this extremity. The air becomes germ-free at a variable distance from the free extremity, depending upon the rapidity with which the current is made to traverse the tube.

If this law holds true for smooth, equal tubes, so much the more certainly must we expect the deposition of dust particles from the air of inspiration to take place in the proximal portions of the respiratory tract. For this apparatus is especially adapted to accomplish the cleansing of the air, by means of its numerous subdivisions and angles, its frequent clefts, crevices, corners, and projections, and also through the fact that it is lined with a moist membrane covered with tenacious mucus throughout. These points have been well elucidated by careful experimental observations upon men, by Aschenbrandt, Paulsen, Kayser, Bloch, and others.

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[*] Journal Exper. Med., 1901.

[†] Amer. Jour. Med. Sci., cxxiv.

Regarding the channel followed by the air inspired through the nose, Paulsen and Kayser agree essentially in the following conclusions. In the normal position of the head the bulk of the current takes a course vertically upward, runs along the posterior surface of the nose, follows the septum along the roof of the nasal cavity, and then falls away again downward. Relatively little air flows through the actual nasal meatuses. The expiratory blast follows in the main the same general path, although the posterior part of the middle meatus, and at times the superior meatus also, are partially followed.

In order to determine the manner of deposition of dust, Kayser had some of the patients breathe finely powdered magnesia. He found that a more or less thick layer of the white powder was deposited at the anterior extremity of the septum, about 1.5 cm. from the tip, and at the level of the middle, or of the upper, border of the inferior ethmoid. From here the white powder ran crescentically upward and downward. The upper meatus and the floor of the nose were completely free, likewise the lower border of the inferior ethmoid; only upon the upper surface and the anterior border of the latter bone were a few isolated granules. On the other hand, the anterior, vertically directed, border of the middle ethmoid, also its lower border, and the labial surfaces of the middle meatus were distinctly powdered. Above the middle ethmoid bone, especially upon the septum, it was possible to see scattered particles. Posterior rhinoscopy revealed some powder in the upper part of the posterior wall of the pharynx, but only where the material was very plentifully employed did it cover the wall of the pharynx from above.

The arched direction of the respiratory current, with the sharp angles at the nasal meatus and at the pharynx, furthermore the dichotomous angles of the bronchi, are of great service in keeping the dust from reaching the lungs. Much depends also upon the character of the inspired particles—on their size, and especially on their hygroscopic quality. Since the air becomes saturated with moisture in the nose, markedly hygroscopic bodies swell up, and are completely sifted out, whereas those of lesser affinity for water are more liable to pass the nose. It is just in the inspiration of the characteristically hygroscopic particles of dried sputum that this factor enters into play as a protective agent. The specific gravity is also important; light bodies float more readily in the air than do heavy ones.

Finally, the experiments show that the deposition depends on the rapidity of the current. The more slowly the air is inspired, the more time is given to the dust particles to find the bottom, and, consequently, the fewer of them reach the trachea and bronchi.

Far more favorable than in nasal respiration are the conditions for the entrance of dust in mouth-breathing. The channel here is both broader and shorter. The first angle in the air-current which arrests a great quantity of dust at the septum narium is lacking. The moisture is less intense—indeed, if we breathe for any length of time through the open mouth, a very disagreeable feeling of dryness soon makes itself evident—and consequently the action upon hygroscopic bodies is less marked. But even here, only a small fraction of the quantity of dust inspired finds its way into the trachea, especially if the mouth be kept only semi-closed, in which position the surface of tongue, palate, and uvula are closely approximated. These mucous membranes are then seen to arrest a considerable quantity of dust (Kayser).

The same laws which control the deposition of dust in general apply also to the bacteria commingled with the air of respiration. The latter are, in fact, nothing more than very fine particles of dust, and are as a rule not isolated but joined to other organic or inorganic particles of dust (Koch). The grounds for this analogy are based not only upon general considerations, but are strongly supported by the investigations of Zaufal, Thompson, and Hewlett. The first-named found that in rabbits the number of germs capable of further growth diminished progressively from the nose to the tubal ostium. The two latter authors found that in the healthy nose the bulk of the bacteria were collected at the introitus, and that the inner portion of the nasal mucosa was comparatively free. Hildebrandt's experiments on rabbits with aspergillus fumigatus led to the same conclusions.

In order to correct the exaggerated notions which prevail concerning the number of bacilli inspired, I think it well to append a brief summary based upon Zarniko's procedures. With every respiration about one-half liter of air is taken in.

	Number of Germs in 1 Liter of Air.	Number Inspired with Each Breath.
According to Hesse:		
In sleeping-rooms after cleaning	18.0	9.0
In sleeping-rooms at night	0.2	0.1
According to Petri:		
In factories at the windows	0.9	0.45
In stables	41.4	21.7

The great majority of the micro-organisms floating in the air of respiration are arrested in the nose and in the nasopharynx, and never reach the larynx. The same holds true of dust-particles, even the very finest and lightest. And yet, notwithstanding the really great protection which they afford, the upper air-passages are not capable of keeping the air of respiration absolutely free of dust and germs under all circumstances. In forced breathing, especially with open mouth, they cannot prevent a fractional part of these impurities from reaching the terminal bronchi and alveoli. This is proved, on the one hand, by the large quantities of coal-dust, stone, sand, and iron particles which are found in lungs at autopsy, and, on the other, by the numerous experiments with these kinds of dust made by Knauff, v. Ins, Ruppert, and Schottelius and Arnold. All this evidence admits of only one interpretation, namely, that these foreign bodies reached this location by way of the respiratory passages. Considerable collections of such particles are found only in adults, while in children and short-lived animals they are lacking, a proof that the condition presupposes years of sojourn in a dusty atmosphere or, as in animal experimentation, an artificially induced over-saturation of the air with dust. If we consider that the amount of dust deposited in the lungs constitutes only a minute fraction of that inspired, we may form some conception of the enormous quantities of dust which in the course of time are taken into the body.

Since the upper air-passages form the main dumping-ground for the inspired dust, including tubercle bacilli, one would expect them to assume a high rank in the order of infection. Yet this, as is well known, is not the case. The lungs are far more prominent in this regard, and the infections of the nose and pharynx are almost lost sight of, especially in primary forms of the disease. This apparent contradiction finds a satisfactory explanation in the actual means of defense, as will be shown more fully in the proper place.

Nasal Infection.—Nasal tuberculosis evidences itself as an ulcer, a tumor, or under the picture of a lupus associated with granulation tissue, or as a combination of all these forms. In 1879 B. Fränkel asserted that he had never seen a case of this kind. The first observation was made by Willigk, 1853, and this was followed by others: Laveran, 1877, Riedel, Spillmann, Tornwaldt, Weichselbaum, Riehl, Demme, Berthold, Sokolowski, Schäffer, Cartuz, Bruns, Michelson, Juffinger, Hajek, and Seifert, so that Mertens, 1889, in a dissertation inspired by Seifert, was able to collect 31 cases, which were increased by Heryng, 1892, to 90. Weichselbaum found nasal tuberculosis twice in 146 autopsies on consumptives; E. Fränkel found it uniformly lacking in 50 cases of phthisis. Bender, however, found the nasal mucosa involved in 33.3 per cent. of the cases of lupus (66.5 per cent. of the cases of lupus of the mucous membrane). Hahn admitted 5 cases of nasal tuberculosis within three months into Doutrelepont's clinic, of whom almost all were strong, otherwise healthy individuals, with the exception of one who had a commencing apical catarrh. The small number of published cases seems, however, to give no reliable picture of the frequency of the disease, since its sluggish course and obscure symptomatology often serve to hide its existence. Moreover, it often imposes itself as a chronic eczema, on account of the accompanying crust and scale formation (Kaposi), and is very apt to be confused with other diseases unless microscopic methods are employed. Many authors have perhaps failed to publish such cases, as remarked by Störk himself, because they regarded them as only of trivial importance.

If we admit that nasal tuberculosis is indeed more frequent than previously seemed to be the case, it is nevertheless true that it does not occur nearly as often as might be expected from the enormous numbers of tubercle bacilli which enter the nasal cavity with the air of respiration. The magnitude of this invasion may be gauged to a certain extent by the very great number of cases of primary tuberculosis of the lung, although here too the result is vastly inadequate to the cause. We are forced to conclude, therefore, that in the nose certain conditions exist, in the presence of which the invasion of tubercle bacilli does not by any means necessarily involve injury to this organ.

One may assume, especially where consumptives careless with their sputum are to be found, that single bacilli are frequently inspired, and, as above shown, are deposited in the nose, while for the most part no injury to the organism results therefrom.

Straus investigated 29 healthy individuals who were largely employed in rooms inhabited by consumptives. He found virulent tubercle bacilli in the nasal mucosa of nine of them, of whom six were orderlies who lived in the hospital, cleaned the floors, and made the beds; one was a chronic invalid (of three such investigated) who lay in the tuberculous ward, and two were physicians and servant-girls (of seven such investigated) who were busied for only a few hours a day in the ward. In seven cases the result was dubious, as the inoculated animals died within a few days of septicemia and peritonitis.

[W. Noble Jones* inoculated into guinea-pigs the nasal secretions from healthy persons who were not brought more closely into relation with consumptives than the average of human beings, and obtained a positive result in 10.3 per cent. of the cases.—Ed.]

In connection with my inhalation experiments with atomized sputum and pure cultures, I noticed that when I opened the door of the cabinet to remove the animals, a heavy mist of the material blew into my face, even though I had previously taken the precaution to discontinue the process. In one of these instances † I was able to demonstrate tubercle bacilli in the nasal secretion which I shortly after voided. Further infection I had studiously avoided by resorting to the most superficial breathing possible, as was my custom in all these researches.

The occurrence of tubercle bacilli in the nose, as indeed in any part of the upper respiratory tract,—pneumococci, for example, are often found in the mouth,—has given rise to the very general impression that these bacteria fail to go on to further development only because the organism resists them. When, however, predisposing circumstances, such as catching cold, arise, it is supposed that these organisms force their way into the tissues, and then give rise to their characteristic forms of disease, pneumonia, pleurisies, and so forth. This theory I consider to be untenable. In the first place, development of the bacteria seems to be opposed in the upper air-passages by the character of the secretion, and it is on this account that we never encounter a luxuriant growth, or actual pure cultures of the pneumococci, even though all the conditions which predispose to infection be present. Physiological and physical factors also oppose the downward growth of bacteria which have become fixed upon the moist surface of the upper respiratory tract, for the current of mucus always sets from below up, and never vice versa, and a separation of the germs from the moistened surface is, according to Nägeli, under no circumstances possible. For all processes originating in the deeper parts, therefore, we must put the blame upon germs carried primarily by the air of respiration to the part itself.

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* Medical Record, Aug. 25, 1900.

† Recently, in another attempt to infect animals with dry pulverized tuberculous sputum, I discovered that virulent bacilli had invaded my nasal canal, as I was able to prove by inoculation experiments, and yet no infection followed in my own case. See Berliner klin. Wochenschrift, 1898, Sitzungsbericht d. Berl. med. Gesellsch.

Is it possible to explain the absence of disease in such cases upon the theory that the predisposition to tuberculosis was lacking? How is it that those individuals who subsequently betray predisposition by falling prey to pulmonary consumption do not at once develop a nasal tuberculosis?

The nose, as the organ most exposed in respiration, is exceptionally well provided with auxiliary agents of defense, for the purpose of overcoming the invading micro-organisms. Upon the septum, where the deposition of germs takes place first, the true skin extends a considerable distance before the lining of mucous membrane begins. None of the mucous membranes, not even that of the eye, or of the larynx, not to mention the bronchi, possess as high a grade of reflex irritability as the nose. Chemical and mechanical stimuli of very insignificant grade produce a most energetic reaction. The vessels become injected, the canal is narrowed, there is a temporary secretion of a watery fluid, partially contributed by the lachrymal glands, and even sneezing may occur. By means of the mucus normally present or increased in this way the bacteria and other dust-like particles are washed away; by sneezing or blowing the nose they are actively carried off; by scab-formation they are incrusted; or, finally, they are hurried toward the anterior or posterior nares, whence they are subsequently expectorated by the vigorous ciliated epithelium which sweeps away all danger much like a broom. The chemical character of the nasal secretion seems to a certain extent to militate against the increase of the bacteria. In the normal nasal secretion there is only a minute number of germs. Wurtz and Lermoyez have determined the fact that even the most resistant of anthrax spores are killed off by nasal mucus within three hours. Almost all other micro-organisms were found to succumb in the same fashion to the bactericidal quality of this mucus. Further hindrances to the invasion of the mucosa by the tubercle bacilli are furnished by the protective film of mucus, by the above-mentioned activity of the ciliated epithelium, and in other situations by the well-developed layer of squamous epithelium.

The nose affords the worst conceivable conditions for the growth of such bacteria as are not endowed with especially active proliferative tendencies, and for the tubercle bacilli, therefore, in particular. It is to this circumstance, and not to a deficient predisposition on the part of the organism as a whole, that we must ascribe the relative infrequency of nasal tuberculosis when compared with the great opportunities for infection.

These conditions are very slightly altered by catarrhs, etc. It is true that the continuity and the resistance of the epithelium is thereby diminished, but this damage is again counteracted by the increased secretion, which bathes the mucosa and washes away detritus so much more effectually.

In addition to the increased secretion associated with certain bacterial processes,—*e. g.*, ozena,—the tubercle bacillus is exposed also to the competition of other germs with which its slow proliferation unfits it to cope with any degree of success.

The hindrances to growth are overcome when large numbers of tubercle bacilli gain an entrance simultaneously into the nose.

At the Surgical Congress of 1889 I had occasion to exhibit an infection of the nose and of the associated submaxillary glands in guinea-pigs, which I had produced by the introduction of pure cultures of tubercle bacilli and of sputum, making use of a pigeon-feather in order to avoid traumatism. [Renshaw* confirmed this observation, and in seven out of eight cases succeeded in producing tuberculosis of the lymphatic glands in guinea-pigs by applying the bacilli to the uninjured mucous membrane of the nose. De Bono and Frisco† brought cultures of tubercle bacilli in contact with the mucous membrane of the nose in rabbits, and in one hour aspirated the aqueous humor of the eye, inoculated it into guinea-pigs, and produced tuberculosis.—Ed.]

Consumptives are exposed more than all others to this danger. Leaving out of consideration the increased danger from inhalation and from contact to which they are exposed, it is very apt to happen to them that sputum particles are driven into the nose. This occurs especially when they choke a cough, keeping the mouth closed at the same time, or when they retch or vomit violently. Consumptives, therefore, contribute the greatest quota to the number of those afflicted with nasal tuberculosis.

Kossel, for example, found numerous tubercle bacilli in the nasal mucus of a girl of nine years, who had died of cerebral and pulmonary tuberculosis; the nasal mucosa showed neither macroscopic nor microscopic changes. Kossel rightly attributed the existence of the organisms to the presence of incompletely expectorated sputum. Thus it is that the care of consumptives and association with them provides opportunities for infection.

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* Jour. of Pathology, 1901.

† Annali d'Igiene Sper., 1901–03.

Liebreich relates the case of a woman of healthy parentage who fell sick of a nasal catarrh after tending a consumptive sister for one and a half years. She then developed a growth in the nose, which persisted and became the starting-point of a lupus of the nasal mucous membrane. Bresgen observed a woman who had tended a consumptive, and who subsequently developed a nasal and a facial lupus.

The arrest of tubercle bacilli upon the mucous membrane and their invasion of it are greatly facilitated by wounds, ulcerations, stagnation of secretions, and obstruction of the nose.

A circumstance which must be held to favor infection is the disgusting habit which many people have of boring into the nose with the fingers. If tubercle bacilli happen to lurk within the nose, or if they are carried in upon the dirty finger or nail, or upon the handkerchief (often spit-covered) which envelops the finger, they are actually rubbed by this means into the mucous membrane. The infection is, of course, so much easier if the epithelial layer is damaged or if excoriations are already present. [Schmitthuisen,* St. Clair Thompson,† and Kiar ‡ have reported cases of primary infection of the nasal mucous membrane which were probably brought about in this way. Rosenburg § concludes that many cases of lupus of the nose originate from a primary infection of the mucous membrane produced by this means.—Ed.]

There is an analogous danger in the bad habit which many children have of introducing all sorts of foreign bodies into the nose. Physicians are not rarely called upon to extract from the nose such articles as peas, or nuts, or orange-skins, chestnut-shells, buttons, cherry-pits, dice, hair-pins, corks, and sponges, some of which have remained hidden for fifteen months (Felici), three years, even as much as twenty-five years (Major).

The septum not only constitutes the chief agent for the arrest of the inhaled dust, but is also primarily exposed to traumatisms of this nature. This, doubtless, affords an explanation of the fact that in the vast majority of the cases the septum, especially its cartilaginous portion, together with the alæ nasi, furnishes the point of origin for the tuberculous process.

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* Jour. of Laryngol., 1900, p. 397.

† Trans. Clin. Soc., London, 1900, p. 829.

‡ Rev. de Laryngol., 1901, p. 263.

§ Jour. of Tuberc., July, 1901.

It is true that in individual cases the etiological connection is not evident, yet the possibility of any origin except through exogenous infection is practically excluded by the numerous observations which have been made, in addition to those previously detailed by Cozzolino, Middlemass Hunt, Beermann, Behrend, Farlow, Wroblewski, Molinie, Chiari, Baurowicz, R. Sachs, and others. As early as 1893, Herzog had described twenty cases which were in all probability of primary origin. As a rule, the victims were strong, hereditarily untainted individuals, who even later showed no signs of tuberculosis.

Syphilitic primary sores of the nose furnish an analogy with this mode of origin. For example, in a case reported by Krelling from Lesser's polyclinic the infection probably occurred through the fact that the patient was massaged for facial erysipelas by a woman who spit upon her fingers to lubricate them for the manipulation. D'Aulney saw a chancre upon the skin of the septum narium extending over to the mucous membrane of the right nasal meatus in a patient who acknowledged that he had used his tongue in illicit intercourse during a number of years.

The conditions in the nose which serve to protect it against invasion from the exterior are naturally unavailing when the tuberculous virus is carried into the mucosa of the nose, so to speak, *a tergo*. For example, it is possible for the lymph-channels to bring the poison from preëxisting neighboring foci.

Neumayer records the case of a consumptive in whom extraction of a tooth seems to have been the point of departure of a buccal tuberculosis. The process extended from the alveoli to the maxillary sinuses and from these to the nose. A similar case, also occurring in a consumptive, is recorded by Rethi, namely, of an oral tuberculosis consequent upon the extraction of a tooth, which broke through to the nose. Dmochowski found that pharyngeal tuberculosis was constantly associated with the same affection of the nose.

We cannot here detail more fully the significance which may attach to nasal tuberculosis as a focus of origin for disease of the neighboring tissues, namely, of the pharynx, mouth, orbits, and of the external skin. Especially to be emphasized is the connection of nasal tuberculosis with tuberculous meningitis, by means of migration of the tuberculous virus along the lymph-channels discovered by Key and Retzius to the subarachnoidal space. (See also the works of Naunyn and Schreiber, and of Schwalbe and Flatau.)

Demme relates the case of a boy of eight months with healthy antecedents, who was adopted into a family of which the father was suffering from acute pulmonary phthisis. The boy fell sick of ozæna tuberculosa, and eventually died of a tuberculous meningitis.

Of surpassing importance is the swelling of the nearest cervical lymph-glands, which often becomes associated with nasal tuberculosis. My experiments, the results of which have been both published and demonstrated, leave no doubt that tuberculous disease of these glands may result from infection of the nose. Not only this, but the nasal mucosa, though affording an entrance to the virus, may itself give no visible evidence of alteration throughout the course of the disease.

An infection of the above-mentioned glands occurs especially in childhood, when the mucous membranes are less resistant and the lymph-channels wider, and a not inconsiderable proportion of the cases of scrofula and of meningitis are undoubtedly attributable to this mode of infection. The mucosa of the nose is just as helpless against an invasion by way of the blood-stream as it is against lymphatic invasion from neighboring foci of disease. Clinically, however, such cases are unimportant, since the organisms, when once they have become free in the circulating blood, ordinarily involve organs far more vitally important, and the nasal condition passes unnoticed.

Infection of the Nasopharynx.—As much of the inspired dust as the septum and the nasal passages have failed to arrest passes in its further course into the retronasal space. Just as at the meatus the air-current again experiences a deflection, an angular turn downward, which serves to precipitate a portion of the dust and the germs in line with the previous course of the current, that is to say, upon the roof of the nose, and upon the transitional area between this and the posterior pharyngeal wall. This fact is well established by Kayser's experiments, who determined that these situations formed a second main depot for the arrest of dust. Only a very small fraction of the dust passes from thence to the trachea.

All that was said of defensive conditions against infection in the nose holds, with very slight variations, of the nasopharynx. Here, too, there is a tough coating of mucus, which arrests the germs (*i. e.*, the dust particles), and is then expelled with them by the active ciliary motion of the epithelium, and by the violent muscular efforts of hawking, coughing, and swallowing. The germs are thus carried to the stomach.

The conditions which influence the settlement of micro-organisms are more favorable in the retronasal space, inasmuch as there is a considerable collection of lymphoid tissue just at the points most exposed to the deposition of germs. This tissue is known anatomically as Luschka's gland, and its surface is broken by numerous furrows, the so-called crypts. Germs which become lodged in these crypts are very apt to retain their hold, inasmuch as the ciliary epithelium is frequently replaced here by a thick layer of squamous epithelium (Dmochowski), and is also damaged by inflammatory processes. Adenoid vegetations, such as are often found in children before the age of fifteen—later, as is well known, they ordinarily undergo a retrograde metamorphosis—may be regarded as furthering local infection in two ways. In the first place, the narrowing of the respiratory channel which their enlargement entails facilitates the deposition of bacilli just at this point, and militates also against their subsequent expulsion; in the second place, the further progression of the bacilli into the depths of the tissues is favored by numerous clefts and rifts in the surface.

Wendt has shown two cases of tuberculosis of the pharyngeal tonsils; Broca, however, failed of a positive result in 100 pharyngeal tonsils which he investigated; Brieger, according to a personal communication, found it only once in a large number of investigations both of a histological and an experimental character.

Dieulafoy produced a tuberculous infection in seven out of thirty-five guinea-pigs, into the peritoneal cavity of which he had introduced pieces of the pharyngeal tonsils. In addition to these experiments, which are not exactly irreproachable in character, tuberculous foci have been histologically demonstrated in apparently healthy adenoid vegetations by Lermoyez in 32 cases, twice; G. Gottstein in 33 cases, 4 times; Brindel in 64 cases, 8 times; Pluder and Fischer in 32 cases, 5 times; total, in 161 cases, 19 times.

It is characteristic that they were found largely in the children of tuberculous parents, that is to say, in children who lived in a contaminated atmosphere.

It is going too far, however, to assert that tuberculosis is the cause of the hyperplasia, as does Trautmann, and thus to make hyperplasia of the pharyngeal tonsils and tuberculosis identical conditions.

In spite of all, we can hardly expect to find a primary tuberculosis, occasioned by respiratory infection, more frequently in the naso-pharynx than in the nose. Its safety lies in the diminished number of germs which reach it, the greater part having been previously filtered out of the air by contact with the vibrissæ, the septum, and the nasal passages.

Primary isolated tuberculosis of the pharyngeal tonsils was found by Suchanneck in the body of a child. Dmochowski has recorded six autopsies with ulcerative retronasal tuberculosis accompanying a fresh miliary tuberculosis of the lung; of these, three in particular (cases 1, 4, and 5) were most probably primary, inasmuch as there was no indication of any other older focus.

It is a striking fact that in all of these cases of presumably primary nasopharyngeal disease a miliary tuberculosis was superadded. The number of cases is too small to permit of a broad generalization, and the facts are, moreover, in themselves insufficient. Although we grant that the abundance of lymph-follicles in the nose would facilitate the absorption of tubercle bacilli by the lymphatic system, and would, in fact, render such a process far more probable than in other parts of the body, nevertheless these bacilli would not pass directly into the thoracic duct or into the vascular system; they would be transported in the first instance into the nearest lymph-glands, which at times serve as very efficient filters. Moreover, experience teaches that tuberculosis of the palatine tonsils is no more frequently complicated by a succeeding miliary tuberculosis than is disease of any of the other organs. Yet the palatine tonsils resemble both anatomically and histologically the tonsils of the fauces, and should, by all analogy, afford the same opportunities for absorption of the bacilli into the lymphatic system.

The five cases of Pluder and Fischer and also the majority of Gottstein's cases are to be regarded as primary, in so far as this interpretation can be established by the negative condition of the organs.

The fact that the retronasal space is far more predisposed to primary and respiratory infections than is the nose itself becomes very evident when we consider the secondary infections. First in importance are the particles of tuberculous sputum which are thrown upon this area by the act of coughing. Ordinarily and under normal conditions in the act of coughing the soft palate is driven against the posterior wall of the pharynx, the so-called prominence of Passavant, and in this manner the nasopharyngeal cavity is closed against the sputum which is thrown up from below. Whether this closure functionates as perfectly in cachectic and emaciated consumptives with somewhat hyperplastic palatine tonsils as it does in healthy and strong individuals is undetermined. At any rate, the closure does not occur with faint or imperfect coughs, or with suppressed coughs, the mouth being closed, and particles of sputum may be carried up into the nasopharynx together with the air which is thus driven through the nose. In the vomiting which so often troubles consumptives, and in coughing with closed mouth, when "something goes down the wrong passage," particles of food of considerable size and partly altered may be carried into the nose. Even though the greater part of the sputum is again thrown out through the nose and the mouth, there is still danger that some portion will remain, and that the bacilli will gain a foothold upon the fornix, which is most exposed to accidents of this character. Here they are apt to develop further, especially if inflamed areas happen to be attacked.

Most often retronasal tuberculosis is found in consumptives, as, indeed, one should expect; moreover, it is not the earlier stages of the disease which are most subject to this complication, but rather the later period, during which the sputum is more copious and more rich in bacteria. E. Fränkel found it ten times (eight times combined with tuberculosis of the organ of hearing) in fifty autopsies upon such cases; Dmochowski fifteen times in fifty-six such cases, among which he found it six times in sixteen cases presenting a coincident laryngeal tuberculosis. Similar secondary complications in consumption have frequently been found by Wendt, Suchanneck, and Koschier.

The explanation for this frequent combination of retronasal and laryngeal tuberculosis is not to be sought in a common predisposition of these parts. Rather it depends upon the fact that the closure of the pharynx above described (musculus thyropharyngeus) does not occur as in the normal act of coughing, but is opposed by the tumefaction of the surrounding tissues which so often occurs in laryngeal phthisis. Furthermore, it is possible that the type of cough, which is hardly less variable in different individuals than, for example, their gait, may play a rôle in determining the invasion of the upper pharynx by particles of sputum.

No further explanation is needed for tuberculous changes in the nasopharynx, in so far as these arise through extension from neighboring foci or by lymphatic invasion. There is likewise no difficulty in accounting for the origin of such foci in consequence of a blood infection, which is, as a rule, evidenced by the other symptoms of an acute general miliary tuberculosis.

[Lewin* in 1899 found evidences of tuberculosis in 10 out of 200 adenoids examined bacteriologically. He believes that the disease is generally latent in this situation and is usually associated with well-marked tuberculosis of other organs, especially the lungs. Baup† inoculated material from forty-five adenoids into guinea-pigs with but one positive result. J. Wright* studied fifty-one adenoids, and in none was he able to demonstrate tubercle bacilli. Lartigau and Nicoll† have made one of the most thorough studies of this subject. They inoculated into guinea-pigs material from adenoids removed from seventy-five individuals. So far as could be determined, the children from whom the material was obtained were all healthy, and free from discoverable tuberculosis. Of the seventy specimens tested, twelve induced tuberculosis in the inoculated animals. They concluded that primary tuberculosis of the pharyngeal tonsils is probably more common than is generally supposed, and that these organs may be a portal of entry for the tubercle bacilli in the production of either localized or general infections.

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* Arch. f. Laryng. u. Rhinologie, 1899, Bd. ix, S. 277.

† Les Amygdales porte d'entree de la Tuberculose, Thèse de Paris, 1900.

Mintz‡ reported a case of tuberculosis of the parotid gland in which the histological findings indicated that the portal of infection was the duct rather than the lymph-channels. The fact that the child's mother was suffering from phthisis gave rise to the belief that the disease had been communicated from her. Lartigau § reported a somewhat similar case in which there was tuberculosis of the submaxillary glands,—apparently here, too, an ascending infection.—Ed.]

Infection of the Ear.—Infection of the nose is closely related to tuberculosis of the organ of hearing, especially of the middle ear.

The frequent occurrence of a purulent otitis media in the course of a phthisis had for a long time made the close relationship of the two processes a probable assumption. The probability became a certainty, when Eschle, Voltolini, Nathan, Schubert, and others demonstrated the tubercle bacillus in the secretions from otitis media, and Habermann found them to be present in the tissue of the tympanum. These claims found ample confirmation. Tuberculous otitis media develops in all stages of pulmonary consumption, even in cases in which this process is in a condition of temporary improvement. At times, it occurs even before any positive symptoms of pulmonary disease are to be made out, but in the majority of cases otitis is associated with far advanced disease of the lungs.

E. Fränkel found the organ of hearing affected sixteen times in fifty autopsies on consumptives, that is to say, almost as frequently as the nasopharynx. Habermann found miliary tubercles five times in the middle, and once in the inner part of the organ of hearing, in twenty-five organs removed from twenty-one consumptive bodies.

The manner in which an ordinary otitis media purulenta arises in otherwise healthy individuals gives the best indication of the origin of the form of disease now under discussion.

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* N. Y. Med. Jour., 1900, p. 508.

† Am. Jour. Med. Sci., June, 1902.

‡ Deut. Zeitschrift f. Chir., Bd. lxi.

§ Med. News, April 12, 1902.

The secretions of an ordinary otitis, according to the earliest investigations of Zaufal, Rohrer, Netter, Gradenigo, and Moos, present especially the steptococcus and the staphylococcus pyogenes, and also the pneumococcus. These organisms, then, are to be regarded as the causative agents in the disease. The simultaneous occurrence of the same bacteria in the oral, nasal, and pharyngeal cavities of diseased, and even of healthy individuals, reveals the very close connection which must exist between these parts and the ear. It is most natural to regard the Eustachian tubes, which provide a direct channel of communication between the tympanum and the nasopharynx, as the path along which micro-organisms pass from one of these cavities into the other. This hypothesis has, indeed, been already broached by Habermann.

It is true, indeed, that the tubes do to a certain extent shut off the middle ear. Whether an infection may occur through the gradual invasion of the bacteria, or whether such a mode of advance is absolutely prohibited under normal conditions of health by the action of the ciliated epithelium of the tubes and by the character of the secretions, is as yet entirely undetermined. It is, however, a certainty that all of the natural provisions of defense are inadequate in the face of certain forced actions: in forcible expiration, in sneezing, retching, vomiting, in catheterization, in the Politzer method of treatment, and in dilatation by bougies. All these things are associated with dilatation of the tubes, whereby nasal secretions and sputum particles, especially if situated upon the margins of the tubes, may be driven violently into the tympanum.

Thus we can blow air into the middle ear through the tubes. Nasal douches are rightly dreaded, because, even with moderate pressure, fluid is frequently driven into the os medium, where it sets up inflammations; in ozena, for instance, Zaufal saw a pneumococcus otitis produced in one case by the Valsalva procedure; in another, by simply blowing the nose. When there is perforation of the tympanum, it is well known that blowing the nose forces a draught of air through the rupture with a hissing sound. A case of E. Baumgarten's illustrates how much force such a column of air may possess: A patient who had had running of the ear from his youth, but in whom this had stopped for a year, blew his nose very forcibly, and at the third blast felt something give way in his ear with a hissing sound. Examination revealed a fresh perforation in the drum.

Even chewing-tobacco may be driven into the middle ear in this manner. Haug saw a patient who, without being a snuff-habitué, once by exception took a pinch, which caused violent sneezing. To escape the ridicule of his friends, he suppressed the expiratory phase of the act and kept his mouth closed. He developed a catarrh of the middle ear, and upon paracentesis the pus was found to contain particles of snuff. Kessel had previously published a similar case. Thus there is sufficient proof of the permeability of the tubes, and consequently a suppurative otitis media should always suggest infection by this route.

Tuberculous otitis is subject to the same conditions. Most of the cases are consumptives. I have shown that it is possible for the tuberculous sputa to find its way into the nasopharynx in such cases. On their way to the anterior nares, the particles of sputum naturally tend to be deposited on the projectile lips of the Eustachian meatus, and are detached with greater difficulty than from the smooth wall of the nose (Dmochowski). All this favors infection. Moreover, the respiratory catarrh present in so many of these cases occasions coughing and sneezing, so that there is no difficulty in accounting for the frequency of tuberculous otitis in consumptives. According to Habermann, who has made valuable contributions to this question, the tubes are wider in consumption, owing to the absorption of the fat and the tissues. According to Eitelberg, the tubes are wider in children than in adults.

Localized tuberculosis of the nose or the nasopharynx is as efficient a cause as consumption. Thus, we not rarely find tuberculous otitis in scrofulous children, whose caseous cervical glands bear evidence of the former presence of the bacilli in their drainage territory, the mouth and nasopharynx. Schwartze has found tubercle bacilli (generally in small numbers) in a large proportion of these cases of scrofulous otitis.

[Many additional cases of tuberculosis of the middle ear followed by mastoiditis have been reported (Goldstein,* Whitehead †). It seems not unlikely, however, that the frequent presence of pseudo-tubercle bacilli in the cerumen may have led to errors in diagnosis where only microscopic examinations have been made and where no animal inoculations have been carried out. For instance, Wingrave‡ found that acid-resisting bacilli could be demonstrated in a large proportion of middle-ear discharges. He examined one hundred cases, finding true tubercle bacilli in seventeen, pseudo-tubercle bacilli in seven.—Ed.]

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* Journal of Laryngology, March, 1903.

† Ibid., April, 1903.

‡ Ibid., March, 1903.

The tubes themselves, though the medium of infection, may escape the disease in case their ciliated epithelium eliminates the germs. But a tuberculous focus in the lungs or elsewhere is by no means a necessary preliminary, as Walb believes, to the entrance of bacilli into the tubes; these canals bring the ear into indirect communication with the external world. There is no difficulty in the theory of a primary tuberculosis of the middle ear which is set up by way of the tubes in healthy persons who have taken bacilli into the nose along with the air of respiration from a tuberculous environment. We need only refer to the evidence furnished by Straus and the author of the existence of bacilli in healthy noses in such cases. Primary tuberculosis of this kind is, however, a rare occurrence, since very few germs find their way to the meatus of the tubes and are ready at the critical moment to be carried by a chance wave into the canals. Haug's case of a primary chancre of the meatus due to the use of an infected catheter suggests the possibility of a tuberculous infection from dirty instruments.

Tuberculosis of the lung and of the middle ear are not necessarily dependent upon one another, but both may independently originate from the same source of infection, although the former will take longer to manifest itself even if simultaneously infected.

The localization of bacilli in the tubes, and to a lesser degree, perhaps, their invasion, is very largely favored by all diseases associated with alterations in the respiratory epithelium, notably measles, diphtheria, and particularly scarlet fever.

Tuberculous infection of the middle ear most frequently takes place by way of the tubes, but may also occur through the tympanum. The carelessness of many persons in cleansing out their ears, for which purpose they use often a dirty finger, or an ear-scoop, or the first thing that comes to hand—a match, hair-pin, crochet-needle, pencil, pen, or even a toothpick, which had perhaps previously been introduced into the mouth by themselves or some other person—affords ample opportunity for the occasional carrying of tubercle bacilli to the drum. If now there is a perforation of this membrane, the road is open to bacteria. Cozzolino asserts that the inexpert use of the ear-scoop is often responsible for perforation of the drum. It is, therefore, easily conceivable that any of these sharp emergency instruments may at times occasion injuries of the drum, and so open up the road to infection.

Let us recall, also, the varied assortment of foreign bodies which have been extracted from the ear, after having been introduced through the simplicity of children, large and small.

I will cite only a few cases from the very copious literature, in order to give an idea of the wide distribution of this bad habit. The following objects are recorded by Boeckh, Marian, Sexton, and others, as having been extracted from the ear: cotton, garlic, melon-seeds, beans, orange-seeds, barleycorns, peas, plum-pits, glass pearls, plugs of paper and of wool, pieces of chalk and of wood, an amber button, the loop of a shoe-button, a willow catkin—in addition to the bugs, chafers, bed-bugs, flies, and maggots which have crawled in without the aid of the victim.

Especially noteworthy is a case of Lallement's. There was a severe otitis media purulenta, produced by a foreign body; after the inflammation had been cured, forty days from the commencement of the condition, a small flat stone the size of a grain of wheat was discharged from the nose in the act of sneezing. This had evidently passed through a perforation in the drum into the tympanic cavity, thence into the Eustachian tube, and so to the nose. It cannot be denied, therefore, that tubercle bacilli may occasionally find their way into the ear by this path.

It is conceivable that infection may be occasioned by a kiss, especially a forcible kiss, upon the ear given by a consumptive. There are cases on record in which this mode of expressing affection has caused perforation of the tympanum. Bürkner and Gruber saw perforations of the drum produced by kissing; Cozzolino, an otitis media serosa induced by kissing and then sucking at the external meatus; Zucker, a primary chancre of the auditory meatus traceable to a kiss.

Even in case the drum is intact, it does not seem to me that one can absolutely deny the possibility of an exogenous infection, as does Zaufal. For, inasmuch as the mucous membranes of the gut (Dobroklonski), of the nose, of the mouth, the conjunctiva, and even the skin, according to my researches, are permeable to the tubercle bacilli under certain circumstances, there seems to be no good reason for believing that the drum alone is immune. It is conceivable that the cerumen might chemically interfere with the growth of the bacilli upon the external surface of the drum and in the external canal.

Invasion of the germs along the lymph-spaces of the mucous membrane—*e. g.*, from the mucous membrane of the tube to that of the tympanic cavity—is to be thought of only in case there are tuberculous foci in the tissues bordering upon the organ of hearing and the tube. Thus, Walb, Ouspenski, and Rieger were able to follow the progress of a lupus from the nose to the middle ear, and Gradenigo from the pharynx to the internal ear.

Occasionally it may occur that the tubercle bacilli find their way from the basis cranii and the cavity of the skull through the petrosquamous fissure into the middle ear, along the prolongation of the dura into that cavity, as has been described in epidemic cerebrospinal meningitis by Klebs, and in one case of simple meningitis by Moos; other paths are also conceivable. The reverse case of migration of tubercle bacilli from the ear into the brain is more frequently realized.

The foregoing discussion has regarded the middle ear as the seat of the tuberculosis. Affections of this region do, indeed, constitute by far the greater portion of the cases of tuberculous disease of the organ of hearing, and are also generally the point of departure for infection of the other parts.

If the tuberculosis of the middle ear develops still further, it involves the drum, and produces a perforation outward. It attacks the cells of the mastoid, leads to caries of the ossicles, invades the internal ear or the labyrinth, or advances toward the tegmen tympani and the squamous bone. All these processes, however, are generally secondary, and constitute the sequelæ of middle-ear disease.

It is only very rarely that the modes of infection thus far described seem inefficient, so that it becomes necessary to postulate a hematogenous origin when, for example, there is disease of the mastoid process without involvement of the middle ear, as described by Wanscher, Schwartze and Siebenmann. Inasmuch as the supposed integrity of the tympanic cavity is based upon clinical evidence and not upon a post-mortem examination, it cannot be held to prove a hematogenous origin. A case described by Knapp is convincing: a child of five years, with multiple tuberculous foci in the bones,—vertebræ, left ankle, both orbital margins, and the left malar,—developed tuberculosis of the mastoid process, while the drum and tympanum were to all appearances normal.

But the fact that the mucosa of the tympanum is normal does not necessarily indicate that the infection has been hematogenous in origin. For, in the first place, it is not inconceivable that tubercle bacilli may be carried into the mastoid antrum from the tympanum along the natural channels of communication, through the agency of a forced expiration, etc. Moreover, all the mucous membranes which have as yet been investigated with regard to this point have shown themselves to be not absolutely impassable to tubercle bacilli; why, then, should not the mucosa of the tympanum occasionally permit the passage of tubercle bacilli, especially in young individuals?

The possibility of a hematogenous infection is not gainsaid. When tubercle bacilli have once invaded the blood-stream, they will also find their way to the arteries which supply the organ of hearing, and will settle in their ramifications, with a frequency which is in direct proportion to the severity of the blood infection.

Schwartze describes such a case: in a woman thirty-seven years old, with an obsolete focus at the apex, the tuberculous process had spread from a peribronchial lymph-node to the left pulmonary vein, and had led to a general miliary tuberculosis, which also involved the tympanum. On the median wall of the round window of the right ear, the mucosa, which was otherwise normal, contained a focus occupied by tubercle bacilli. Such conditions will, however, always be an object of anatomical rather than of clinical and medical interest.

Frequently the auricular and cervical glands corresponding to the ear take part in the tuberculous process, as I have regularly found to be the case in otogenous infections in guinea-pigs. In this way they constitute a part of the symptom-complex of scrofulous lymphadenitis. Ferreri asserts that the large incisura Santorini of childhood facilitates the extension of inflammatory affections from the ear to the glands, the parotid, and the articulation of the jaw.

Infection of the Larynx.—Laryngeal tuberculosis is protean in appearance. It may take the form of miliary tubercles*; more frequently, however, of infiltration, or of ulceration secondary to this, its character having been demonstrated by the finding of tubercle bacilli by B. Fränkel. Tumors of tuberculous origin were first described by Ariza, Tobold, Mackenzie and Schnitzler, and have since been observed by many writers (Avellis). Finally there is the lupoid form, which is not very rare, and was recognized by Virchow.

As has already been shown, the air of respiration is so thoroughly filtered in nasal respiration that only in very exceptional cases can the larynx be infected by bacilli introduced by this route. In mouth-breathing the danger is greater. Bacilli introduced in this manner, and not penetrating deeper, are driven upward and outward by the ciliary epithelium which is everywhere present except on the posterior wall and on the vocal cords. If the bacilli are attached to large particles of dust, the latter produce a reflex increase of secretion which is adequate for the removal of even large-sized particles.

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* The laryngoscopic demonstration of tubercles in the larynx is not so old. In 1881, Schnitzler found it worth while to record a case of this kind as proof of its existence.

We find that in case of streams all obstructions in the bed disturb the even flow, and occasion acceleration, slowing, and eddies. The same holds true of the larynx. This constitutes, not a regular tube, but a channel interrupted by folds, clefts, and projections, which interfere with the steady upward progression of the mucus, and cause a blockage of the stream in places, with resulting accumulation and deposit of the bacteria.

Large amounts of irritant dust, especially that which is chemically irritant, increase the reflex to the point of inflammation, and this predisposes to the formation of small fissures and epithelial erosions (erosive ulcers of Virchow) in those parts which are subject to marked tension, particularly in forced vocalization and coughing. Other diseases, *e. g.*, syphilis, act in the same manner.

Thus it is that although far fewer bacteria find their way to the larynx than into the nose, and in spite of the protection afforded by the ciliated epithelium and the mucus, which may be even increased to meet emergencies, tubercle bacilli do occasionally find their way to the larynx, and, having once entered the tissues, they continue to multiply rapidly. This possibility finds its most pregnant expression in the cases of primary tuberculosis of the larynx, the occurrence of which, though long disputed, has been definitely established by the casuistics of recent years.

Primary tuberculosis of the pharynx, which is hardly explicable except as an infection by inhalation, is established beyond cavil when even the autopsy fails to disclose any other focus. Such a case was demonstrated by E. Fränkel: The patient first came under his care in 1880. The disease involved the vocal cords, subsequently extended to the posterior wall of the larynx, and proved fatal five and a half years later, in 1885, after having produced extensive destruction of the organ. The autopsy disclosed isolated, apparently fresh tubercles in both lungs, but no trace of caseous or broken-down foci, no trace of pleurisy, and no adhesions; the lymph-nodes of the lungs were neither enlarged nor caseous.

This was an undoubted case of primary tuberculosis of the larynx. Fränkel refers to a similar case of Orth's, in which the lungs were absolutely free.

Massucci had previously reported three cases as evidence of the existence of a primary tuberculosis of the larynx, in which the autopsy by Macchiafava had failed to disclose any pulmonary lesion. Demme's famous case does not seem to me to be free from objection. In so far as the theory of a primary laryngeal tuberculosis is based upon clinical evidence, it is open to the objection that there may actually be some minute primary focus in the lung which has escaped detection.

Cases of apparent primary laryngeal tuberculosis, in which either the patients were under observation for a short time only, or fell sick, or even died, within a few weeks or months, of pulmonary phthisis, as described by Jullien, Boylan, Dehio, Neidert, Fischer, Cadier, Jores, and others, are not to be regarded as necessarily primary.

On the other hand, cases in which pulmonary involvement occurred very late or not at all, make it probable that the primary focus was in the larynx. Thus, Trifiletti described the case of a girl twenty-one years old with tuberculous infiltration of the laryngeal mucosa and apparently healthy lungs; eight months later the apices gave the first symptoms of a broncho-alveolitis.

Josephsohn described a case from the clinic of Kafemann, of a girl of eighteen with tuberculous growths on the larynx, who gave signs of phthisis only after two years had elapsed. Panzer described a case in Chiari's practice, of a fibroma of the cords which had been operated on two years previously, had recurred in four months, and which turned out, upon examination, to be tuberculous in nature. The patient remained in good health. In a case of de Renzi's, a primary laryngeal tuberculosis took root on a syphilitic base. Lupus has been observed as a primary affection in the larynx by Ziemssen, Haslund, Obertüschen, Garré, Martin, Langie, Garel, Moritz and Barth.

The more frequent the invasions of tubercle bacilli and the greater their number, the oftener will the means of defense prove inefficient, with a corresponding increase in the number of infections. The consumptive is especially exposed to this danger, since in him the larynx is traversed day and night, for months or years, by large quantities of infected sputum. Thus the greater number of patients with laryngeal tuberculosis are consumptives. The following statistics give the frequency with which the larynx complicates pulmonary tuberculosis: Kruse, among 742 tuberculous cases, 123 times, 16.6 per cent.; Gaul, among 424 pulmonary cases, 113 times, 25.7 per cent.; Eichhorst, among 462 autopsies on consumptives, 130 times, 28.1 per cent.; Heinze, among 1236 autopsies, 376 times, 30.6 per cent.; de Lamallerie, among 502 cases of phthisis, 222 times, 44.2 per cent. Wagner asserts that laryngeal phthisis occurs in 33 per cent., Bosworth in 30 per cent., of all cases of pulmonary consumption.

The care which one should exercise in the interpretation of such figures is illustrated by a report from the General Hospital of Vienna. Of 1936 cases of pulmonary tuberculosis, laryngeal tuberculosis required treatment in seventy-five, or 4 per cent., whereas in the Rudolph Hospital only 0.4 per cent. showed involvement of the larynx. The explanation of this difference lies in the fact that the Rudolph Hospital maintains no separate laryngological division, in consequence of which most tuberculous cases with hoarseness find their way to the General Hospital.

Rice has shown to what extraordinary conclusions one may be carried by statistics. This author finds that one-fourth of all death certificates show pulmonary phthisis, and since statistics show that the larynx is in a similar condition of disease in about one-third of these cases, he comes to the conclusion that one-twelfth of all patients (Author) who come to treatment suffer from tuberculosis of the larynx.

The theory of certain authors that laryngeal tuberculosis is not due to the contact of the mucous membrane with the sputum, but is, as a rule, hematogenous in origin, lacks all foundation in fact. Hematogenous infection of course occurs, but this is by way of exception, and is ordinarily found only in general miliary tuberculosis. In general, the very localization of the tuberculous foci in the larynx is opposed to such an idea. With hematogenous infection, we should expect an equal distribution over the entire area of mucous membrane supplied by the vessel at fault, and not an especial predilection of certain spots for the tuberculous virus, as is clinically the case. To explain this upon the basis of a difference in the predisposition of the parts—a favorite argument—does not avoid the difficulty. For these more favored areas lose their apparent immunity as soon as a focus develops in their proximity, so that they become liable to invasion. They then succumb just as rapidly and as easily as the more "predisposed" areas.

The unequal localization is, however, easily explained on the theory of sputal infection. The much-plicated interarytenoid space is the favorite site, and it is just here that sputum is actually compressed against the mucous membrane in the act of vocalization; secondly, the free edges of the vocal cords, where the same process occurs; then, the upper surface of the vocal cords, which do not easily admit of being cleansed on account of the absence of ciliated epithelium; and, finally, the processus vocales, the prominence of which tends to interfere with their cleansing. The posterior wall also, which Keller, by means of the Kilian method, found to be diseased in thirty-four out of forty-eight cases of laryngeal phthisis, is very evidently an especially exposed situation, particularly in bed-ridden patients, since the sputum lies there for some length of time during the suspension of the reflexes at night.

According to Gaul, the distribution of tuberculous ulcers of the larynx in 113 cases was as follows: 53 times the true cords; 36 times the posterior wall of the pharynx; 27 times the epiglottis; 17 times the arytenoid cartilages; 6 times the anterior wall of the larynx; 5 times the sinus of Morgagni; twice the false cords; twice the cartilages of Santorini.

Infection from the surface of the mucosa is further indicated, as Fischer points out, by the occurrence of contact ulcers on corresponding parts of the larynx, which continually touch one another, *e. g.*, the processus vocales. In short, those places in which the sputum tends to stagnate, and points of prominence, which are especially exposed to insults in coughing and expectoration. This condition is best expressed by the term "exposed," since "predisposed" denotes something subjective, and may easily give rise to misunderstanding. In the same way, one speaks of a post of peril as exposed to bullets, not as predisposed to them.

The fact that the larynx is often diseased upon the same side as the lung has been interpreted as evidence of predisposition on the part of the entire corresponding half of the body. Schäffer noticed that many persons displayed a paresis of one of the vocal cords, often discoverable only after prolonged and exact observation, and hoarseness in the evening, in advance of any symptom of tuberculous disease of the lung. Weeks or months later a focus would develop in the lung of the same side. Although Schäffer has perhaps exaggerated the frequency of the phenomenon, since he claims to have found it in 74 out of 110 cases, or in 67.2 per cent., nevertheless his explanation, based upon Luschka, seems very rational. He assumes that tubercle formation in the apex of the lung, which is not yet sufficiently advanced to reveal itself by other signs, may exert pressure on the recurrent nerve, which lies between the apex and the arch of the subclavian, and so indirectly occasion a paresis of the corresponding laryngeal muscles. Similar paralyses may be caused by the pressure of enlarged tuberculous bronchial glands, and will then also lie upon the same side as the diseased lung. It is self-evident, as Schäffer says, that mucus and sputum are less rapidly eliminated on the paretic side owing to less perfect functioning on the part of the muscles. Hence, the side in question is subject in increased degree to the danger of infection.

Kurkunoff interpreted the histological findings as bearing out the theory of an infection by way of the lymph- and blood-channels rather than by means of the sputum. He examined twelve tuberculous larynges and found tubercles in apparently healthy parts in the subepithelial layers, or even deeper. As he asserts, the bacilli decrease in numbers toward the free surface of the organ, and in some cases do not even reach the epithelial layer. From this he concludes that the bacilli do not work their way into the mucous membrane from the exterior.

In the first place, this conclusion is by no means unavoidable, and is, moreover, in direct contradiction to other facts. I have shown experimentally that the bacilli can make their way through the normal mucous membrane, that they can even penetrate to the lymph-glands, without leaving any palpable evidence of their transit; Dobroklonski demonstrated the same fact histologically of the intestinal mucosa. Kurkunoff, consequently, puts himself in the position of denying that invasion from the surface may give rise to an experimentally induced tuberculosis of the lymphatic glands, or to a subepithelial tubercle of the gut from purposely infected food. As Trasher says, there is no necessity of assuming that the epithelial layers of the mucous membrane must first succumb to the infection, and the absence of bacilli in the superficial layers affords no ground for denying an extraneous infection.

Moreover, Kurkunoff's finding is not to be regarded as typical. On the contrary, in the examination of sixteen tuberculous larynges, E. Fränkel found that the ulcers showed enormous numbers of tubercle bacilli toward the surface as well as toward the center of the ulcerated tissues, and also that the infiltrated posterior wall of the larynx showed a surface epithelium thickly studded in all its layers by tubercle bacilli. The same author found numerous bacilli in the proximity of one of the ducts of a gland, whereas they could not be found in the deeper layers.

Bacilli, having once penetrated to the deeper layers, will naturally proliferate more rapidly than in the epithelial layer, which offers them a certain amount of resistance, and in this way they give color to the misconception entertained by Kurkunoff. The latter formed his impressions from well-advanced conditions, whereas Fränkel's investigations on early lesions demonstrate that the invasion of the bacilli takes place by way of the epithelium.

E. Fränkel was not able to confirm the theory of an independent morbid process in the acinous mucous glands, which has been considered by some as a preliminary to the tuberculous infection (Rindfleisch, Möller, Heinze, Gouguenheim, Tissier). Indeed, it would be rather extraordinary that bacilli should settle at the mouths of the ducts, just where the mucus streams forth.

Another point opposed to the theory of the hematogenous origin of laryngeal tuberculosis is the fact that all other symptoms of a bacillemia are lacking, and that any other foci which develop are situated in places subject to infection through the sputum, *e, g.*, the intestinal canal.

The importance of this question is not forensic, but eminently practical, for if the enemy attacks from behind, through the blood-stream, we are powerless to meet him. If we cure one focus, another will rise up to take its place. On the other hand, the theory of a sputal infection has suggested a number of useful and important measures.

Infection by means of the sputum is especially favored in consumptives by the following circumstances: In the first place, the reflex cough excited by the presence of the sputum irritates the mucosa of the larynx, and, if very severe, may even induce inflammatory processes which lead to the destruction of the epithelium. The sputum is forcibly driven against the inferior surfaces of the epiglottis, processus vocales, and the folds of the larynx, and acts as a mechanical trauma. If the sputum is delayed in its passage outward, *e. g.*, at night, or through voluntary restraint, it exercises an erosive action in time, breaks down the epithelial barrier, and opens the portals to the bacteria. The continual passage of sputum serves also to dull the sensibility of the mucous membrane and to delay the reflexes adapted to its removal, in exactly the same fashion as is done by frequent sounding, a manipulation formerly resorted to by way of preparation for endolaryngeral operations. At all events, the reflexes become heightened again as soon as erosion and ulceration occur, and the nerve-endings have become exposed. Finally, however, the general loss of tone leads to a paresis of the ciliary epithelium. Thus it is that the frequency of laryngeal complications, which are often entirely revealed by autopsy alone, directly corresponds with the age of the pulmonary processes, increasing as the end approaches.

Gottstein advanced the theory that laryngeal ulcers were always either tuberculous or luetic, and never catarrhal, but this view has been overthrown by the observations of Heryng (once on his own person), of Schnitzler, and Maure. Nonspecific ulcerations may occur in the larynx of the tuberculous, either alone, or simultaneously with specific erosions, as has been shown by Masini, among others, and by E. Fränkel, by histological methods. They are, of course, exceptional, since they can scarcely escape infection from the sputum, as it passes over them or tarries on their surface, so changing their original character. On the other hand, it is going to the other extreme to regard catarrhal erosions as the necessary antecedents of tuberculous ulcerations (Lacke), since the permeability of the uninjured mucous membrane has been amply demonstrated.

Syphilitic changes likewise furnish a means of invasion for the tubercle bacilli. Combinations of the two processes have been described by Irsai, B. Fränkel, Schnitzler, Grünwald, Arnold, Rice, Helwes, Luc, Havilland Hall, etc.

It is asserted that phthisical women often acquire laryngeal tuberculosis after the puerperium. It may be that forced crying during the delivery induces lesions of the laryngeal mucosa, which facilitate the invasion of the passing bacteria.

Frequently the course of events is reversed, and tissues already affected by tuberculosis are invaded by other bacteria, although they are unable to overcome the resistance of the healthy tissues. These mixed or secondary infections may also markedly influence the course of the disease. Thus, E. Fränkel determined the presence of staphylococci and streptococci in thirteen out of eighteen cases, and stated that he "invariably found tubercle bacilli in deeper layers of the tissue than the pyogenic germs, so that, apparently, the latter took advantage of the injury wreaked by the former in the tissues." This description exactly parallels my own findings in cases of secondary infection of the lungs.

Laryngeal tuberculosis may be set up by lymphatic transmission from a neighboring focus, *e. g.*, in the palate, fauces, or tonsils. Lupus, in particular, tends to travel considerable distances along the lymphatics of the skin and mucous membrane, yet fails to reveal itself by pain. O. Chiari and Riehl examined 68 persons who suffered from lupus either of the face or the mucous membrane, but gave no subjective symptoms of laryngeal disease, and discovered lupus of the larynx in six female cases. Holm determined the presence of laryngeal disease in five out of fifty cases of lupus, Haslund in ten out of 109 cases of lupus vulgaris (9 per cent.), also females.

Cases of laryngeal lupus are recorded also by Grossmann, Schley, Middlemass Hunt, Smith, Massei, Schrötter, Serrede, etc. As a rule, the transmission occurred from neighboring areas of mucous membrane or skin. A tuberculous focus of the larynx itself becomes a source of further infection, either by contact, as of symmetrical portions of the larynx, or by lymphatic extension to neighboring organs, either of the mouth or the pharynx. This assertion hardly demands casuistical demonstration. The lung is particularly exposed, inasmuch as the deep inspirations which follow paroxysms of cough are very apt to detach infected particles of tissue, which then becomes firmly lodged in a small bronchus—a fact which should not be overlooked in the treatment of laryngeal tuberculosis, notably by curettement. Such an accident may become of great moment even in the presence of a preëxisting pulmonary tuberculosis, since large numbers of active bacilli may thus be aspirated into healthy portions of the lung. The consequences reveal themselves, indeed, only after the lapse of months, so that a causal connection is with difficulty established.

In this connection I may relate a case which I treated in 1885 in Görbersdorf. A lady with tuberculosis of the lungs and larynx presented certain tuberculous excrescences in the larynx, and these were to be operated upon, at Brehmer's suggestion, by Gottstein in Breslau. On the eve of her departure I again determined the conditions. The next day she returned, with the explanation that Gottstein had found nothing to operate on in the throat. Upon examination, I discovered that the excrescences had disappeared. The patient admitted that during the trip she had noticed that something in her throat had become detached, but that she had not spit anything out. Shortly afterward the patient left Görbersdorf, and died not long thereafter. Post hoc! Propter hoc?

Infection of the Trachea and Large Bronchi.—In the trachea most of the conditions which favor infection in the larynx are lacking—the irregular conformation, and the compression of the sputum in the intercordal and interarytenoid spaces. The trachea is a simple, smooth, wide-open tube, the walls of which never come into contact. Moreover, it is better protected, by virtue of its greater distance from the nose and the mouth, from the invasion of germs carried by the air of respiration. The surface is protected by a layer of mucus, which is carried upward, together with everything which it has arrested, by ciliary activity of great power, and thus eliminated. Therefore, it does not present any deposits of carbon-dust, even though the air be laden experimentally with enormous quantities of dust.

An idea of the activity of the ciliated epithelium may be obtained by the well-known experiment with the pharynx and esophagus of a freshly killed frog, which is split open and spread out smoothly on a cork. If, then, small particles of coal-dust or cork are placed on the surface, which should be kept moistened with physiological salt solution, they may be seen to be transported steadily in one direction.

Kraft has found that the ciliated cells are also mechanically irritable, and that dust excites their activity. Furthermore, in investigating the air-ducts of warm-blooded animals, he found that the results varied according as they were in a condition of catarrhal inflammation and heavily coated with mucus, or were simply covered by the thin fluid mucus normally present. In the former case the cilia were sluggish, the wave of irritation traveled slowly, and was far more susceptible to all sorts of chemical influences; the normal cilia, on the other hand, operated much more actively and energetically.

The tracheal and bronchial mucosa, moreover, has the advantage of a very sensitive apparatus, which induces reflex cough when irritated by the presence of dust or foreign bodies, as has been shown by the experiments of Nothnagel, and thus serves to eliminate unwelcome invaders. Primary tracheal tuberculosis, due to infection from the air, is, therefore, extremely rare. The only recorded case to my knowledge is that of Valette.

Even if there be a pulmonary tuberculosis, the bacilli of the sputum are scarcely able to find a vulnerable point. The sputum is hurried past the inflamed areas, with their injured epithelium, by the thick layers of mucus.

Only *sub finem vitæ*, or at autopsy, is tracheal tuberculosis more frequent, but even then it seems to be of relatively recent occurrence, and is not associated with any extensive destruction. Toward the end of life, of course, reflex activity is in abeyance, the sputum travels upward more sluggishly, and so has an opportunity to erode and destroy the epithelium by virtue of its chemical constituents, thus preparing the way for the invasion of the bacilli. Consequently the ulcerations are generally superficial, often of considerable extent, and occupy the posterior surface, which in bed-ridden invalids is the most exposed.

Mackenzie described a tuberculous growth above the bifurcation. Schmiegelow, a pea-sized mass of tuberculous granulations on the anterior wall of the trachea, one centimeter below the rima, associated with diffuse infiltration of the larynx. Whipham and Delépine believed that they had seen the lupoid form. It is possible that the latter is frequently transmitted from the larynx by way of the lymphatics, and escapes discovery by reason of the difficulties attending the examination.

The wall of the trachea is exposed at certain places to the danger of infection from without, particularly from caseous bronchial glands. Against these its elaborate internal mechanism is of no avail. Aside from certain other observations (Riegel), erosion of the trachea, or of the large bronchi, by caseous bronchial glands has been described by Meynet, Poland (with erosion of the esophagus), Tait, Lundis and Wallis, Loeb (with a collation of previous cases), Gulliver, Parker and Biggs. Most of the individuals were very young. Nowack's case, however, was sixty-one years old, and Barry's was a woman of seventy-one. Otto relates the rupture of a Pott's abscess into the trachea. The bacilli do not, as a rule, go much further, for the scene is closed by death, which may be caused either by asphyxiation through the lodgment of masses in the air-passages, or by a hemorrhage, as in Barry's case, in which the glands had perforated the trachea, the bronchus, and finally the vena cava.

Petersen rescued a boy from this accident by a speedy tracheotomy; the subsequent course is not recorded. The conditions influencing infection are the same in the large, stiff-walled bronchi as in the trachea, except that diminution of caliber encourages the detention of small remnants of viscid tuberculous sputum, and so tends to set up tuberculous processes.

Infection of the Lung.—The infection of the lung is the most important chapter in the study of tuberculosis; indeed, one of the most important in the entire pathology of the human body. Although the tubercle bacillus became recognized in a very short time as the causative agent in all those processes which are accompanied by typical tubercle formation, and which are found to be identical with analogous artificial lesions in animals, nevertheless certain difficulties were met with in the explanation of pulmonary tuberculosis. It is true that a number of clinicians, notably Rühle and Lichtheim, quickly adopted the new conception of the origin of the disease, that it is an infection by the tubercle bacillus through inhalation; moreover, a certain proportion of them explicitly renounced the older doctrines. But the theory of "constitutional anomalies" was very firmly entrenched. For many of the older generation it was altogether too difficult a task to surrender the notions which they had cherished for years, and which were to all appearances well grounded, adopting in their stead the new-fangled theory of infections. Thus it was that the attempt was made to "put new wine into old bottles."

There were a number of circumstances which seemed to throw doubt upon the identity of tuberculosis with caseous pneumonia, *i. e.*, consumption, and which appeared to assign to it a secondary position, the rôle of a parasite in a previously diseased tissue. In the first place, several investigators in a large number of cases failed to demonstrate tubercle bacilli in caseous pneumonia, either through faulty technic or lack of training in the method. Moreover, though the disease is the very prototype of consumption, tubercle formation seemed, microscopically at least, to be an unimportant factor in its pathology; further experiments upon animals resulted in the production not of a cheesy pneumonia with cavity formation, but of a general miliary tuberculosis. Finally, the erroneous belief in the ubiquity of the tubercle bacillus gave color to the theory of a secondary implantation upon the lung.

The idea was (Dettweiler and Meissen) that if chronic pneumonia did not quickly resolve, caseation ensued in those areas most completely deprived of their vascular supply, which thereby became transformed into nutritive media for the ubiquitous bacillus.

The disease was thought to be only complicated by the bacillus, not produced by it; phthisis was a disease *sui generis*, which originated through a variety of injuries to the lung, but not through infection.

Biedert and Siegel expressed themselves to the same effect. "The ordinary type of chronic phthisis results from the secondary implantation of bacilli upon a previously established chronic pulmonary infiltration; the disease cannot, therefore, be regarded as an infectious disease in the ordinary sense of the term."

These theories appeared untenable in the light of the facts established by Koch's investigations, but they were entirely overthrown by the further developments of the modern theory of infection. Not only did improvements in technic result in the more and more frequent discovery of tubercle bacilli in the very earliest stages of phthisis, but Baumgarten established the identity of tubercle and caseous pneumonia from a histological point of view. The objection had been made that in animal experimentation a generalized infection was produced, whereas among human beings the process was, as a rule, localized in the lung alone. This, however, could easily be overruled by a comparison with the exactly similar conditions which govern the manifestations of the anthrax bacillus; in animals it produces a general infection, in men ordinarily a localized pustula maligna, and yet there is not the slightest doubt as to the real identity of the two processes. It is even more striking that the great differences which exist between the various syphilitic phenomena—a syphilitic dermatosis, a gumma, an exostosis, and a bubo, for example—do not militate against the conception of a single and uniform cause for all of them. Furthermore, it was shown that caseous pneumonia, and even cavity formation, may be elicited in animals by means of an experiment calculated to reproduce the conditions which control infection in human beings, that is, by the aspiration of tuberculous fluids. A part of the phenomena associated with phthisis are also explicable as due to a mixed infection. Finally, the belief in the ubiquity of the bacillus was shown to correspond with the actual facts. As a natural consequence of these investigations, the opposition to the theory of the infectious nature of the disease became continually less pronounced. Other conceptions of its character which were at the time seriously advanced are to-day hardly worthy of momentary consideration. Such were, for example, the idea of Gregg, that the cause of the disease was to be sought in the diminished albumin-content of the blood; of Bouchardat, who believed that the tubercle bacilli sprang into life within the body of their "host," and were not invaders; of Mays, who regarded pulmonary consumption as a neurosis of the vagus nerve; or of Liebreich, who considered that the actual rôle of the bacillus in the disease was undetermined, even as late as the year 1895.

For the vast majority of the cases of phthisis the lung and its associated bronchial glands are either the sole focus of disease, as evidenced by the cicatrices so frequently found at autopsy, or are easily recognizable as the primary focus when compared with the more recent and younger manifestations in other organs. Pulmonary tuberculosis is generally, therefore, a primary disease, from which it follows that it arises through infection from without, the only possible carrier of the infection being the air of inspiration.

On first thought it may seem somewhat paradoxical that the upper air-passages, the nose, pharynx, and larynx, are as a rule only secondarily diseased, although they are the parts which are chiefly exposed to infection from the deposition of dust, while the lungs, which are further removed and should *à priori* be less susceptible to invasion, are the favorite seat of primary disease.

Indeed, we should be rather inclined to doubt whether the very small diameter of the terminal bronchioles, which varies between 0.3 and 0.4 mm., would permit the access of dust and germs to the alveoli, were it not that daily evidence of this fact is afforded by the histological condition of the lungs of coal-miners and stone-cutters. Naturally, this difficulty is hardly of moment as regards the bacillus, which measures only 0.0015 to 0.004 mm.

The conditions governing the inhalation of dust afford a very simple explanation for this apparent difficulty. If we examine a lung shortly after such an inhalation, we find the major part of the dust in the upper passages, progressively less in the lower passages, and in the lung itself least of all. In a few hours, or at most days, the upper passages are again absolutely free from coal particles, which have been eliminated by the ciliary epithelium and the current of mucus. The deeper passages, however, are found to retain a not inconsiderable portion of their small quota of coal-dust, which in course of time is slowly and incompletely transported by way of the lymph-channels to the bronchial glands.

The movement of mucus within the respiratory tract is exactly like the current in a system of water; just as the fountain-heads and the rivulets lack the power of the great streams to which they are tributary, so too the mucus of the finer air-channels fails to sweep along foreign particles with the power of the current in the larger bronchi and trachea. Moreover, the ciliary epithelium, which is a powerful aid in removing foreign bodies, is absent in the alveoli, so that these latter form a sort of storehouse for the dust particles. When they have reached this goal, there seems to be no remedy but their removal by the lymph apparatus, which finally deposits them in the bronchial glands. It would really seem as though nature had not fashioned the human organism for a life of civilization, for only such a life is accompanied by a great a amount of dust inhalation.

In so far, therefore, as concerns the elimination of dust particles, the terminal air-passages, and especially the alveoli, are in a very unfortunate position, notwithstanding their protected situation. The continuous inhalation of dust-laden air in the course of years leads to a very considerable accumulation of this material in the deeper parts, while the upper passages retain barely a trace.

Exactly the same conditions govern the inhalation of tubercle bacilli. Here, too, the greater number of the inspired bacilli are deposited in the upper passages, and are again swept outward by the current of mucus. The opportunity for permanent localization is afforded only in places in which the stream is dammed back or delayed, as by fissures, or ulcerations, or clefts, or trabeculæ. The very same opportunity is afforded, however, in a pronounced degree to those few bacteria which have penetrated to the deeper parts. Here they tend to remain permanently, even under normal conditions, by reason of the very inadequate natural provisions for their removal. Tubercle bacilli behave in exactly the same manner as do inactive particles of dust, such as fragments of coal or of stone, and this affords a proof of the fact that purely mechanical conditions, and not special idiosyncrasies, govern the localization of the infection in the lungs.

Fortunately, the tubercle bacilli, especially when virulent, are vastly more rare than are, for example, particles of coal-dust. In the atmosphere at large they are swiftly and incessantly destroyed by the action of light. As a rule, they are found in considerable numbers only in the dwelling-places of consumptives. Even here there are numerous factors, notably the dryness and the activity of the air-currents, which are of extreme importance in desiccating and pulverizing the sputum and in throwing the bacilli into the atmosphere. All of these factors are ordinarily just as much underestimated as the distribution of virulent bacilli in the air is overstated.

As a proof of the importance of the humidity of the air, I may relate the following occurrence. I once pulverized some dried sputum in a somewhat moist cellar; upon the succeeding day, when it was to have been used for inhalation, I found only agglomerated masses, which were useless for the purpose in hand and consequently without danger. A further proof is afforded by the failure of previous experiments in inhalation, owing to the superabundant moisture of the atmosphere. I invariably succeeded in these experiments simply by imitating the conditions which prevail in nature.

Sojourn in infected places does not necessarily imply the deposition of bacilli in the body, at any rate the terminal air-passages. Of course, the more prolonged and frequent such a sojourn, the greater is the probability, *ceteris paribus*, of such a mischance. The individual himself controls the chances to a certain extent, in so far as infection depends on his manner of breathing, whether nasal or oral, whether superficial or deep.

It is impossible to determine whether the bacilli invariably settle and multiply after reaching the alveoli, or whether the body possesses means for preventing this. We observe not the invasion of the bacilli, but only the final effect thereof, the disease itself. We found that inhalation, especially of fairly large quantities of bacteria, was invariably followed by infection in animals, even in those not very susceptible to the disease. Guinea-pigs developed tuberculosis after the inhalation even of small numbers of germs, of which not all were virulent. We shall consider this question, in so far as it concerns human beings, in the chapter on Infection, under the head of Predisposition. Here we are interested only in the fact that such infection is possible; is, indeed, enormously frequent.

Practically, there is ample evidence of this possibility. First, there are many hundreds of animals (the author alone having contributed several hundred) who regularly fell sick after the inhalation of tuberculous material in moist or dry condition. Then, there is existence of this material in a shape fit for respiration in the environments of consumptives. Finally, there is the overwhelming frequency of tuberculosis of the lungs among men exposed to just such a manner of infection.

Nowadays, the inhalation theory has become the common possession of almost all physicians. For the sake of completeness, we may refer to certain contradictory theories. Thus, Volland asserts that pulmonary tuberculosis arises through an invasion of the lungs by bacilli coming from the cervical glands, rather than along the respiratory tract. The bacilli are carried thence within the bodies of the leucocytes, by way of the main lymph-stream and the lesser circulation. Once in the lung, the leucocytes become stimulated into activity by the abundance of oxygen, and become attached to the walls of the blood-vessels by their pseudopodia. The blood-current tends to break up all such adhesions, but in general anemia there is a slowing of the stream, and the leucocytes are enabled to retain their hold, especially in the apices of the lung, and the bacilli to proliferate.

Roosevelt, too, finds the inhalation theory too simple. He denies that infection occurs directly by inhalation; and holds that the bacilli are carried from the various portals of entry—mouth, nose, wounds, etc.—by the blood-vessels, reaching first the vena cava, then the right heart, and finally the apices. They are supposed to travel along the upper wall of the vessels, because their specific gravity exceeds that of the blood-serum!

The fallacies of such hypotheses are evident from the facts already discussed. When bacilli which have been inhaled gain a foothold, tubercle formation results. The favorite situation of such growths is the mucosa of the small bronchi (Virchow), the terminal bronchioles at the point of transition into the infundibular passages, and the partition walls of the alveoli, where cylindrical epithelium comes to an end and passes over into the flattened epithelium of the pulmonary alveoli (Neelsen).

The subsequent fate and the further distribution of the bacilli have already been considered in their pathological bearings.

Occasionally, instead of going on to development within the alveoli, the bacilli find their way through the mucous membrane, and are carried by the lymph-stream to the bronchial glands, which drain the lung. They may, of course, become arrested at any point in transition. The permeability of the normal pulmonary mucous membrane for the bacilli was stated by Flügge to be absolutely controverted by certain experiments of his which were probably inadequate. This permeability followed as a logical corollary from Arnold's demonstration that indifferent forms of dust were passively transported along the same channels; further, from the analogy with other mucous membranes (Baumgarten, the Author, Dobroklonski), and finally was settled beyond doubt by the fact that Buchner proved it to hold for the far larger organism of anthrax.

This manner of transportation of the bacilli occurs to a far greater extent in children than in adults, owing to the facts that in early life the mucous membranes are less impassable, and also that the lymph-channels are proportionally of greater caliber. For these reasons it is more frequent in children than in adults to find tuberculous foci in the bronchial glands, while the lungs, the portals of invasion, remain intact. It happens not rarely that the glandular capsule is broken through, in cases of diffuse cheesy degeneration of the glands, and that the neighboring parts of the lung are secondarily overrun by bacilli. Such foci betray their origin by their situation at the hilus, near the glands, in contrast to the general location of primary disease, namely, at the apices.

In the lungs of adults, on the other hand, the tissue of the mucous membranes is firmer, and the lymph-channels are narrower. Moreover, numberless lymph-channels are blocked, like the pores of a much-used filter, by particles of coal, of stone, and of dust, as is evidenced by the microscopic appearance of such a lung. Thus, bacilli which have gained the alveoli are forced to develop *in situ,* for lack of any path of egress.

As the proliferation of the bacilli in the alveoli goes on, a certain number of the micro-organisms find their way into the lymph-channels, and secondarily involve the bronchial glands.

To resume: in childhood infection through the respiratory tract finds its expression chiefly in primary tuberculosis of the bronchial glands; in later years, in primary foci in the lung itself. Both affections are genetically identical. Klebs, however, is inclined to refer the infrequency of phthisis in childhood to the high blood-pressure in the infantile lung. Influenced by this circumstance, a number of authors have ascribed a secondary rôle to infection *per inhalationem* in childhood, and have magnified the importance of intestinal infection. Klebs even claims the greatest degree of frequency for this mode of infection.

Practical experience, however, is opposed to this conclusion. Thus, Demme says: "In childhood, nay, even in the very first year of life, inhalation tuberculosis is more frequent than intestinal tuberculosis, and the bronchial glands are especially the seat of infection. Biedert shares the same view. Rauchfuss observed that nine-tenths of the tuberculous children in the Foundlings' Asylum of St. Petersburg suffered from disease of the lungs and bronchi, and Klein found a similar proportion in Moscow (Rauchfuss). Flesch found that the bronchial glands were intensely affected in a third of all cases of tuberculosis in children. The lungs, also, invariably presented either isolated or confluent tubercles, although the changes here were of much more recent date than in the bronchial glands.

Carr, too, is of the opinion that in childhood tuberculosis is apt to begin in the lymph-glands, especially those of the interior of the body, and that it is distributed thence to the lung, *per contiguitatem.*

Abelin considers the bronchial glands as the focus to which the infectious virus is first attracted, and from which it is subsequently distributed. He bases this belief on the fact that he has never observed a case of miliary tuberculosis or of tuberculous meningitis with which there was not associated severe disease of these organs.

From all that has been said, it follows that inhalation tuberculosis is of primary importance in childhood as well as mature age.

In accounting for the almost unexceptional localization of primary pulmonary foci in the apices, one is confronted by the fact that all parts of the lung get an equal proportion of the bacilli, which are equally distributed through the air of respiration. This difficulty has been met by the theory that by far the greater number of invading tubercle bacilli is destroyed by the vital forces of the organism, and that they undergo dissolution either in the parenchyma of the lung itself or in the lymph-channels (Bollinger); whereas the apex constitutes a *locus minoris resistentiæ.* This especial susceptibility is held by some to be due to insufficient respiratory effort; by others, deficient blood-supply and poor nutrition; and by those who wish to be absolutely sure, both factors alike.

We are not, however, in possession of any facts bearing upon the destruction of the tubercle bacilli by the vital forces. Indeed, the process of cure seems to depend not so much upon the destruction of the bacilli, as upon the encapsulation of the living organisms. Moreover, proof is lacking that the apices are deficient either in nutrition or in respiratory activity. On the contrary, Hanau has maintained that the apices inspire well, as a necessary consequence of which they are in an excellent position to take up dust with its associated microorganisms. He emphasizes their weak and insufficient expiratory power, which favors the detention and further development of the bacilli *in situ.* The other parts of the lung, thanks to their position within the thoracic cage, are far less yielding than the apices, and are not able to avoid the effect of expiratory pressure; the dust and germs are therefore more rapidly eliminated, and have no opportunity to develop. Thus the character of the tissue, whether more or less susceptible, has really nothing to do with the case.

Strongly against this theory of an "apical idiosyncrasy" is the fact that healing processes are by far the most frequent just in this area, and also that in children the bacilli traverse its mucosa, despite this "predisposition," and leave it unharmed, only to attack the bronchial glands, and from thence to be distributed to the "less susceptible, better nourished" median portions of the lung, near the mediastinum.

[Two notable publications have recently appeared bearing upon the question of the pathogenesis of pulmonary tuberculosis.

Behring* believes that the disease is in most cases the result of an infection acquired during early infancy through the use of tuberculous milk—an infection which has remained latent until later life. He believes that hereditary or acquired predisposition is an important agent in calling into activity such a latent focus. He considers that the infant's milk is the chief source of pulmonary consumption. He quotes Roemer, who finds that albuminous bodies pass through the wall of the alimentary canal, and into the blood and lymph unchanged in newly born foals, calves, and other animals, while in adults they must be previously digested.

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* Deut. med. Woch., Sept. 24, 1903.

Behring fed anthrax bacilli to adult guinea-pigs, and found that these passed through the alimentary canal, and did no harm. Guinea-pigs less than eight days old, however, after the ingestion of these bacilli, died just as quickly and certainly as by other modes of infection. He also fed attenuated anthrax bacilli to newly born guinea-pigs, and subsequently found them in the blood.

Ribbert,* as a result of his study of the lesions in the lung and in the bronchial lymph-nodes in pulmonary tuberculosis, concludes that most cases of pulmonary tuberculosis are hematogenous. He believes that the original infection is by inhalation; that the bacilli, passing through the pulmonary tissues,—just as in the case of particles of coal-dust,—find their way by the lymph-channels to the bronchial lymph-nodes, and here may set up a tuberculous inflammation. From this situation they are later carried by the blood-stream to the lung, usually to an apex, and there produce the lesions of pulmonary consumption. He believes that if the disease were generally caused by direct inspiration, the pulmonary lesions would be found in a farther advanced stage than those of the bronchial nodes, while the contrary is generally the case.

Ribbert suggests as an explanation of the choice of the apex as a site, the existence of a local anemia, a retarded lymph-flow with the ossification of the first rib which results in hindered movement. He further suggests that most tuberculous inflammations of other parts of the body are probably the result of a hematogenous infection from tuberculous bronchial nodes, admitting, however, that positive proof of this statement is not possible. He says that direct inspiratory infection of the lungs is possible but not probable, except when many bacilli are inhaled at once, an in animal experiments. Natural predisposition, whether hereditary or acquired, would enter as an element in either case.

The above claims are of great interest, but require further confirmation before they can be accepted.—Ed.]

We are justified in laying this amount of emphasis upon the purely mechanical factor, as we find soot deposited most frequently, although not invariably, in greatest amount in the upper portions of the lung (Arnold). Further, Arnold found in his experiments with the inhalation of ultramarine that animals which were exposed to brief inhalations of a not very heavily laden atmosphere, and also animals which were killed after a more or less brief period, showed a more pronounced pigmentation of the upper than of the lower lobes, and of the right than of the left. Similarly, the more frequent involvement of the right side may be explained by the greater width of the right bronchus, which facilitates the entrance of dust, that is to say, bacilli.

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* Deut. med. Woch., April 24, 1902.

All conditions which favor the entrance or detention of bacilli, or which oppose their elimination, are to be regarded as furthering the infection of the lung. Among these belong especially mouth-breathing, since by this means fewer germs are arrested in the upper passages and the path to the alveoli is also shortened, permitting more germs to travel downward. Mouth-breathing, otherwise under the control of the will, is made necessary by pathological affections, such as render the nose and the nasopharynx more or less inflexible. Among these are to be reckoned catarrhs with free secretion, as they often occur in children, also new growths, and especially adenoid vegetations.

Further, infection is promoted by all processes in the lungs which lead to stagnation of secretions, or which are associated with ulceration or desquamation of the protecting epithelium. Very free secretion may, under certain circumstances, facilitate the removal of bacilli.

Not rarely one finds that pulmonary tuberculosis is associated with lues, cancer, and lepra. The small number of data at hand does not seem as yet to warrant the assumption of an etiological connection between these diseases.

Finally, dust deposits, whether of carbon, iron, stone, or lime, are to be regarded as agencies of infection, first because the fragments wound the epithelium with their sharp edges; second, because they furnish aid to the bacilli in securing a foothold, like a *caput mortuum*. These dust particles play a rôle of varying importance according to their character, and according to the degree of irritation, chemical or mechanical, which they excite.

Reich has described an unusual mode of pulmonary infection. A highly phthisical midwife was in the habit of forcing asphyxiated infants to breathe by blowing air into their mouths. Thirteen children upon whom she had practised this method within thirteen months, died with the symptoms of an acute febrile bronchitis and a tuberculous meningitis, while within the same period not a single child delivered by a midwife of the same locality had presented these symptoms, and only three in nine years had perished of tuberculous meningitis.

One is often met with the assertion that pulmonary tuberculosis may be due to "infectious kisses." This seems to me almost incredible. For, in the first place, the saliva is ordinarily germ-free; and, secondly, if particles of sputum are actually transferred from the mouth or the beard of one to another, they do not reach the lung, but are confined to the lips, or at best penetrate to the digestive tract or to the corresponding lymph-glands.

A secondary infection of the lungs, in addition to that already mentioned as starting from the bronchial glands, may be due to the existence of a tuberculous focus in the upper part of the respiratory tract, from which particles or secretions are carried to the deeper parts by forced respiration. For, in addition to this, secondary infections occur *per contiguitatem,* and are brought by the lymph-channels from neighboring organs.

Hematogenous infection, to which an inordinate importance was once attached, is really an associated phenomenon in general tuberculosis, occurring with a considerable degree of frequency, indeed, inasmuch as the etiological condition—namely, a rupture into the vascular system—ordinarily involves a vein, of which the pulmonary capillary system is the terminal filter.

After the detailed discussion which has been devoted to the tuberculous infection of those organs which are in direct connection with the external world, we may dispose in rather brief fashion of the closed portions of the body, inasmuch as their infection is invariably communicated from the former organs.

[Recent experiments by Flügge,* Moeller,† Heymann,‡ Kirstein,§ Hillier‖ and others have conclusively proved that not only is sputum a source of infection when dried and pulverized, but also when disseminated by coughing in the form of small drops or spray. While it is impossible to determine the exact relative importance of these two sources of infection, yet it must be admitted that probably both are of much practical import.

Heymann made use of a glass cabinet into which consumptives coughed, and in which at varying distances dishes and plates were placed for the purpose of catching the droplets that were ejected in coughing. These were then rubbed with a small amount of sterilized broth, which was injected into guinea-pigs. In this way he attempted to establish the distance to which the bacilli may be projected in coughing. The result of his experiments indicated that most of the droplets are large and settle quickly, but that some may remain in the air more than an hour. He found the duration of life of the bacilli in these droplets was eighteen days in the dark, and three days when exposed to light. The experiments of Flügge, Moeller, Kirstein, Hillier and others point to the same general conclusions.

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* Ztschft. f. Hyg. u. Infktionskr., Mar. 2, 1899; Berliner klin. Woch., May 22, 1899.

† Ztschft. f. Hyg. u. Infktionskr., 1899.

‡ Ibid., Bd. xxxviii, 1902.

§ Ibid., Bd. xxxix, 1902.

‖ Brit. Med. Jour., March, 1903.

It may be concluded that under ordinary circumstances the zone of danger from a coughing consumptive extends to a distance of about three feet, but that at times the infective spray may be carried much further by draughts.

Ravenel* collected small particles of sputum disseminated by tuberculous cows in coughing, and proved by inoculation experiments that they contained virulent tubercle bacilli.

The demonstration of the above facts has led to the practice of urging consumptives to hold a handkerchief before the mouth when coughing in order to protect those near them from the danger of infection.—Ed.]

INFECTION OF THE SEROUS MEMBRANES.

Infection of the Pleura.—Tuberculosis of the pleura is almost unexceptionally secondary, and is most frequently associated with tuberculosis of the lungs or bronchial glands. It is therefore directly referable to a respiratory infection. Just as the earlier, widespread conception of an idiopathic pleuritis, due to colds, etc., became constantly more and more restricted in its applicability, so, too, the theory of an isolated tuberculous pleurisy has been gradually narrowed down, so that to-day it can hardly be sustained at all, in face of the findings of pathological anatomists.

As regards the frequency of tuberculous pleurisy, some authors have been inclined to regard almost every pleurisy as of tuberculous origin.

Kelsch and Vaillard were able to demonstrate the tuberculous nature of the pleurisy in sixteen cases, comprising a number of very hale individuals, by the post-mortem findings. In these cases a cure had apparently been achieved, so that they recognized only a tuberculous form of the disease, in addition to those cases associated with sepsis, articular rheumatism, carcinoma, and the chronic diseases of the blood.

Bowditch and Fiedler opposed this rather exclusive theory upon the ground that many cases of pleurisy were not subsequently followed by pulmonary tuberculosis. Further studies have shown that serous and purulent pleurisies are largely due to streptococci, the pneumococci of Fränkel, and staphylococci; but that such as are sterile are mostly attributable to the activity of the tubercle bacillus. These results are due to the work of A. Fränkel, Weichselbaum, Netter, Levy, Barrs, Kiener, Prince Ludwig Ferdinand, Jakowsky, Sacaze, Goldscheider, Fernet, Ihne, and others, who have particularly occupied themselves with the etiology of pleurisies and with the demonstration and cultivation of the associated micro-organisms. [Hodenpyl,* in an important communication, concludes that miliary tuberculosis of the pleura without involvement of the lung tissue, and showing a marked tendency to spontaneous healing, is more common than is generally supposed. He examined critically the pleural surfaces of the lungs from ninety-one adults who had no pulmonary tuberculosis, and in nearly fifty per cent. of these he found in the pleura, by gross and microscopic investigation, nodules and patches which he believed were the result of tuberculosis.—Ed.]

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* University of Pa. Med. Magazine, Nov., 1900.

Schlenker found that of 85 cases in which the folds of the pleura had become adherent, 61 showed more or less marked macroscopic evidence of tuberculosis of the lungs and bronchial glands, a coincidence which does not absolutely demonstrate an etiological relationship, yet offers a strong indication thereof.

The demonstration of tubercle bacilli in the pleural exudate is rarely possible, but has been accomplished by Kelsch and Vaillard, Gombault and Chauffard, v. Eiselsberg, Ehrlich, Kuscharky, Fränkel, Renvers, Netter, Pansini, Prince Ludwig Ferdinand, Grawitz, and others. That the bacilli are so rarely to be found in the exudate has been explained in divers ways. The suggestion has been made in this case, as also for the sterile pus of carious vertebræ and of old cheesy glandular foci, that a spore form is present. This theory, however, is opposed by the negative result of the intraperitoneal injection of such exudates in animals. Grawitz, for example, achieved a positive result in only one out of ten such injections, and Sacaze succeeded only after injecting 25 gm. of the exudate, as suggested by Kiener, whereas small quantities failed to excite a tuberculosis. The cause may very well lie in the small number of bacteria present, since they grow very poorly, as is well known, in fluid media. Indeed, their oxygenophilic property interferes with any growth except such as is maintained at the surface. Further, they tend to sink to the bottom of the fluid, and the aspirated fluid is therefore apt to be free from germs. Their existence is also often betrayed by the fact that the rapid absorption and cure of such exudates is frequently followed by the development of an acute miliary tuberculosis (Litten), or by tuberculous disease of the bones and joints (Czerny), which points very strongly to the absorption of bacilli into the blood-stream. Finally, it is possible to conceive of the origin of such exudates through the simple diffusion of proteins and toxins from cavities.

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* Med. Record, June 4, 1899.

[There is a growing tendency to regard most cases of primary or idiopathic serofibrinous pleurisy as of tubercular origin. As new methods of demonstrating the nature of inflammatory processes are discovered and put in practice, their results, as a rule, tend to render the relation of tuberculosis to these pleural affections more and more important.

Debove and Renault* filtered pleural effusions and injected the filtrate into phthisical patients, obtaining positive tuberculin reactions. Wolff,† Widal and Ravaut,‡ Gulland,§ Barjon and Cade|| and others centrifuged pleural and other effusions, and studied the cellular elements by differential staining—a method to which the term *cytodiagnosis* has been applied. Their results correspond in general in pointing to fairly characteristic differences in the cellular elements of such exudates according to the pathogenesis of the inflammatory process.

In tubercular cases, in the first three days of the process, the exudate contains chiefly polymorphonuclear leucocytes, but after the third day small lymphocytes appear, and rapidly increase in number until they soon come to form the chief part of the cells in the fluid. In no other form of exudate is this marked preponderance of lymphocytes present.

The application of cytodiagnosis has tended thus far to uphold the view that most cases of primary pleurisy are tubercular.

More recently Andre Jousset (quoted by Behring ¶) describes a new method of studying inflammatory exudates, which he calls "Inoscopy." He digests the coagulum artificially, centrifuges, and inoculates the sediment into animals. He uses as a digestant the following:

Pepsin	1–2 gm.
Glycerin	
Acid. hydrochlor. (22 Baume) āā	10 cc.
Sodii fluorid	3
Distilled water	1000 cc.

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* Soc. Méd. de Hôp. Paris, 1891.

† Zeitschft. f. klin. Med., 1901; Fortschritte der Med., April, 1902.

‡ Soc. de Biol., 1901, p. 648.

§ Scottish Med. and Surg. Jour., June, 1902.

|| Arch. gen. de méd., Aug., 1903.

¶ Deut. med. Woch., Oct., 1902.

He claims by this method to find tubercle bacilli in almost all cases of serous pleuritic exudate, and in that from many cases of peritonitis.—Ed.]

The infection of the pleura, its invasion by bacilli, generally proceeds from the lung, in that the micro-organisms are derived from a superficial pulmonary focus. Since, however, the soluble bacterial poisons are diffused more rapidly through the tissues than are the bacteria themselves, it follows that the actual perforation or invasion is generally preceded by productive and adhesive inflammation of the pleura, which is an almost invariable accompaniment of superficial tuberculous foci. On the other hand, bacilli may find their way into the pleural cavity before adhesions have had a chance to form, and thus give rise to a more or less diffuse inflammation. This occurs with especially rapid multiplication of the tubercle bacilli, or with lesions; for example, trauma.

Now and then, especially in old foci,—cavities or glands,—other bacteria, including the pyogenic forms, may find their way into the pleural cavity, and so modify the clinical picture (Sacaze, Ihne). These too, however, tend to sedimentation, in so far as they lack independent motility, yet not to so great an extent as do the tubercle bacilli. They form a flocculent, cloudy mass which floats at the bottom of the fluid, and are, therefore, comparatively easy to demonstrate.

Such a pleurisy may arise even in the earliest stage of a tuberculosis, and may be derived from the primary tubercle in the lung.

In other cases the pleurisy arises through the invasion of bacilli from an adherent bronchial or mediastinal gland, a fact which serves to explain the frequency of pleurisies in scrofulous individuals. All conditions which tend to weaken or to rupture the capsule of such a gland—namely, inflammatory tumefactions such as occur especially in measles or scarlatina, and also traumatisms—are indirectly responsible for the development of a pleurisy.

It has long been recognized that a trauma may be the starting-point of a pleurisy, but the explanation has never been satisfactory. The theory of a predisposition on the part of the pleura has ordinarily been offered to account for such cases.

Invasion of the pleura by bacilli may also proceed from the peritoneum, either through continuity or through contact, by way of the lymph-channels or tissue spaces which traverse the diaphragm, or by perforation (Senator). I had an especially favorable opportunity to study the pathway from the peritoneum in a number of my inoculated animals.

Finally, caries of the vertebræ or of the ribs may occasion a pleurisy. Heath, for example, observed a caries of the eleventh dorsal vertebra with a psoas abscess, which communicated with the pleura posterior to the diaphragm (perforation), while the lung was free.

Infection of the Pericardium.—The pericardium is relatively infrequently the seat of tuberculous disease, as might be expected from its protected position. As a rule, it becomes infected from a neighboring tuberculous focus, most frequently from the pleura, although caseous bronchial and mediastinal glands (Kast), and especially certain small glands lying upon the anterior layer of the pericardium and at its site of reflection, occasionally furnish the starting-point of infection. These glands, on the other hand, derive the poison from their drainage territory, which is the area of contact with the external world (Weigert). Zenker observed a case in which a mediastinal gland had perforated simultaneously into the pericardium and into the esophagus. Pericarditis may also be caused by caries of the sternum, of the ribs, and of the dorsal vertebræ, as also by the perforation of a cavity of the lung. Only recently Meltzer described a macrotubercular form of tuberculosis of the pericardium.

Infection of the Peritoneum.—The peritoneum is exposed in far greater degree to the danger of infection. Tuberculosis of this membrane follows, as a rule, one of two types. In the one it is accompanied by a widespread formation of free connective tissue, with multiple adhesions between the various viscera; in the other it is associated with profuse exudative processes.

Very frequently the disease starts with the perforation of caseous mesenteric or retroperitoneal glands. The process becomes diffused by means of the peristaltic activity of the intestine, or, when adhesions have previously formed, becomes localized.

In the same fashion tuberculous ulceration of the intestines may give rise to disease of the peritoneum, especially the slowly perforating type of ulcers. In cases of sudden perforation a rapidly fatal peritonitis is set up by the micro-organisms of decomposition, which pass out at the same time.

Genital tuberculosis, especially in women, is very frequently the point of departure for a peritoneal tuberculosis. The bacilli are especially apt to find their way out of foci situated in the distal extremity of the tubes, unless the peritoneum has been previously walled off by formation of false membrane. The organisms find their way either through a free opening or through the lymph-spaces in the mucous membrane, notwithstanding the opposing action of the ciliated epithelium of the tubes. In the same fashion pericarditis has been seen to originate through the migration of gonococci into the tubes, and from there into the pelvis (Charier). Indeed, various writers have maintained the existence of a primary, non-tuberculous peritonitis, without associated disease of any of the other organs, occasioned, it is supposed, by the migration of micro-organisms through the tubes, perhaps in connection with the menstrual periods (v. Leyden). Since women seem especially predisposed to infection by virtue of the existence of this pathway of infection, it would seem reasonable to expect the disease to occur with greater frequency in that sex. The ordinary form of peritonitis is found, according to Cruveilhier and Fiedler, with especial frequency in girls, but there is some difference of opinion upon the subject of tuberculous peritonitis. While some of the writers maintain a preponderance in the female sex, others leave the question in doubt (Pertik). Still others assert that it occurs with even greater frequency in men (Sick). The statistics based upon operative cases indicate a predominance of cases in the female sex. They do not, however, give a true picture, since women with tuberculous peritonitis are frequently operated under the false diagnosis of ovarian tumor (König), and frequently resort to the "enterprising" genus of gynecologists and surgeons, whereas the men remain in the internal clinic (Czerny). The number of cases is also very often too small to be of value in drawing general deductions. O. Vierordt, for example, found that of 24 individuals, four times as many men as women were afflicted with the disease.

The male genital apparatus provides a far less permeable route for the tubercle bacillus, yet may also serve as a pathway of invasion. This is shown by the derivation of gonorrheal peritonitis from an epididymitis by means of the migration of the germs through the vessels of the plexus spermaticus, through the ampullar end of the vas deferens, and through the lymph-vessels of the vas described by Horowitz and Zeisel (Horowitz).

In connection with peritoneal tuberculosis we must also consider tuberculosis herniosa. The first observation dates from Cruveilhier; Lejars, Jonnesco, and Bruns collected the cases amounting to 18 up to 1892 (Haegler). Ordinarily the case was one of enterocele or of epiplocele of long standing, and the sac, more rarely the contents, was the seat of the disease. As far as accurate data are forthcoming, in almost every case a general peritoneal tuberculosis was present, and the disease of the hernial sac constituted only an associated phenomenon. Only in a single very briefly described case of Cruveilhier's, and also in a clinically observed case of Haegler's, did the disease seem primary in the hernia. Bruns has energetically disputed the theory of a predisposition on the part of hernias for tuberculosis, on the ground of its infrequency in those structures. He refers, further, to a statement of Albert, who found two cases of peritoneal tuberculosis in which the hernia itself was not involved.

Haegler indicates the following as the most frequent modes of infection. (1) Tuberculous mesenteric glands, with migration of bacilli from the gut; (2) direct infection from the diseased intestinal wall; (3) invasion of the peritoneum by bacilli from neighboring foci, from the pleura through the diaphragm, or through the large abdominal glands. Further, he mentions the widely accepted theory of infection by way of the genital canal in women (Lindner).

The fact that the lower parts of the hernia present the more advanced tuberculous changes, and that nodules become progressively smaller and more scattered toward the neck of the sac (as in Haegler's case), does not argue against a secondary infection from the general peritoneal cavity, since the non-motile tubercle bacilli tend invariably to seek the lowest level of a cavity. The same tendency is displayed in the rectovesical fold and in the pouch of Douglas.

We have already mentioned the transmission of tuberculosis from one serous membrane to another, for example, from the pleura to the pericardium and the peritoneum, and *vice versa*. Such cases, with regression of the disease in other organs, have been carefully studied by Vierordt and others. Usually one has to deal with healthy individuals of mature age, over twenty, without hereditary taint or phthisical habitus.

In case of rupture of a tuberculous focus into the blood-stream, the serous membranes may participate in the general disease, with the formation of multiple miliary tubercles.

INFECTION OF THE UROGENITAL SYSTEM.

Tuberculosis of the urogenital system, the character of which was first established by the demonstration of bacilli in the urine of the dead by Lichtheim, and then *in vivo* by Rosenstein and Babes, Smith, Mendelsohn, Irsai, and others, is in most cases secondary, being as a rule a sequela of pulmonary phthisis. The following statistics give information concerning its frequency and concerning the involvement of the various organs in the disease.

Simmonds found that in fourteen cases of urogenital tuberculosis the kidneys were involved nine times, the urinary bladder thirteen times, the prostate twelve times, the epididymis twelve times, and the seminal vesicles thirteen times.

Von Krzywicki under Neelsen found tuberculosis 499 times in 1250 autopsies; of these, twenty-five were cases of urogenital tuberculosis, that is to say, five per cent. of the total number. He investigated twenty-nine cases, most of which were accompanied by phthisis. Of these, fifteen were males; in them he found that the prostate was involved fourteen times, the seminal vesicles eleven times, the vas deferens four times, the epididymis ten times, orchis seven times, peritoneum three times. In the fourteen females the tubes were involved eleven times, the uterus seven times, the vagina in no case, the urethra once, the bladder in three cases, the ureter three times, the renal pelvis three times, the ovaries once, the peritoneum in seven cases.

Heiberg found in 2858 autopsies eighty-four cases of urogenital tuberculosis, of which twenty-nine were primary, fifty-five secondary, with the following distribution:

	PRIMARY.		SECONDARY.	
	Male.	Female.	Male.	Female.
Urinary organs alone	1	3	7	7
Genital organs alone	5	5	13	8
Both sets of organs	10	5	13	7

Study of these statistics indicates that the disease takes its origin in most cases not from the kidneys but from the genitals, and that urogenital tuberculosis is ascending in character. All those parts which belong to the uropoietic system figure to a lesser extent. This impression is strengthened by observation of individual cases, and of the course they run. This conception is almost universally adopted. Steinthal, however, has championed the descending character of urogenital tuberculosis, that is to say, a course running from the kidneys to the genitals. He bases his belief upon twenty-four cases, for the most part collected from the literature, which do not invariably give complete details regarding the condition of the genital organs, as, indeed, Steinthal himself admits. Recently he has been reinforced by Wandel, with 13 cases, clinically observed. It is not as yet clear in what manner the ascent of the bacilli to the kidneys is accomplished, whether by direct transmission along the surface, or through the lymph-channels of the mucous membrane, or by means of a regurgitation of the infected urine resulting from relaxation of the musculature. At all events, Lewin's and Goldschmied's experiments have shown how easy it is for matter to be carried from the bladder to the kidneys along with a back-flow of urine, and Courtade and Guyon have confirmed their results. Even if this ascending course be admitted to hold good for the majority of cases, there still remain certain observations which seem to speak for a tendency toward descent from the kidney to the bladder. That such a tuberculosis might be set up by the bacilli carried in the descending urine is self-evident. It is true that the deposition of germs is to a certain extent opposed by the frequent washing out which these organs undergo, and by the large amount of fluid which runs past, yet these obstacles are only relative.

Since, then, tuberculosis of the urinary apparatus is mostly secondary to that of the genital system, we shall first investigate the latter.

The theories concerning certain special questions, especially from a statistical point of view, are very contradictory, owing to the fact that the material at the disposal of the individual observer has not been ample enough to warrant any definite statistical conclusions.

For special questions I refer to Runneberg (descending), E. Fränkel, Leichtenstern, Schmidtlein, Routin (bladder tuberculosis), Güterbock, Benda, Durand Farvel, Kirstein, Przewosti, Kümmel, Steinheimer, Gredig, Mann, Pasquier, Freyhan, Lewin, Duret, Brown.

Infection of the Genital Organs.—Observations upon genital tuberculosis, which was previously considered a rarity, have been considerably increased since attention has been especially directed thereto and the diagnosis facilitated. So Kiwisch found the female genitals affected in one of every forty women dying of phthisis; Cornil in one out of every fifty or sixty.

As in the other organs, here too tuberculosis occurs in the form either of miliary nodules or of diffuse caseating and ulcerating infiltrations. In the uterus polypoid excrescences have also been observed, similar to those in the nose or the larynx. The lupoid form has been repeatedly observed.

Kontrin has described a lupus vulgaris of the penis and scrotum; Meissner has described a lupus of the penis combined with one of the face. Chiari has observed tuberculous ulcers of the vulva and vagina; Cayla has described an esthiomenus vulvæ in a forty-two-year-old, advanced consumptive, the anus and vagina forming a single cloaca; Macdonald describes three cases of lupus of the vulvo-anal region, in part with pronounced destruction of tissue, and he further refers to three previous communications from other authors. To Peckham and Lewers, further, we owe a case of lupus vulvæ; the hypertrophic and perforating form has been found by Haberlin;

Viatte has recorded a case of lupus vulvæ, and Sänger a lupus vaginæ of a robust woman of fifty-six, who had borne fourteen children. Katte has described a case similar to the latter with the finding of tubercle bacilli. Taylor records a case of lupus proceeding from the cervix, which extruded over the external genitals; Zweifel records a lupus uteri.

In many of the cases, especially the earlier ones, it is possible that there is confusion with syphilomata or elephantiasis. But Hyde goes too far in concluding that the diagnosis of lupus must *à priori* be false, on account of the absence of all other lupoid manifestations, the rapid course of the disease, and the advanced age of the patients.

It was previously the custom to regard the epididymis as the part most frequently attacked in the male sex (Simmonds, E. Fränkel). More recent researches, however, indicate the prostate as the site of origin of the process, and give it a place of greater importance. According to v. Krzywicki, it was involved in fourteen out of fifteen cases, and the seminal vesicles, epididymis, and orchis followed, in that order of frequency. In childhood the orchis is more frequently involved then the epididymis, just as in syphilis (Hutinel, E. Fränkel).

In the further course of prostatic tuberculosis, which has also been described by Kuhn, Alexander, Vaughan, and Morton, the process extends to the seminal vesicles (Desnos) and to the epididymis (Guyon), or, finally, as we shall see later on, to the bladder.

In the female sexual apparatus the tubes are most frequently affected, then the uterus, the ovaries, the vagina, the cervix, and least frequently the vulva (Whitridge). Among Mosler's forty-six cases, the tubes were involved thirty-four times, the uterus almost as often.

For orientation upon this subject, I refer to the contributions of Revillod (uterine tuberculosis), Orthmann (*pyosalpinx tuberculosa duplex*), Sachs (tuberculosis of the uterine adnexa), Haidenthaler and Williams (tuberculosis of the portio), Cullen (tuberculosis of the endometrium), also Zweigbaum (tuberculous ulcers of the vulva, vagina, and portio), v. Krzywicki and Spencer Wells, Baumgarten, Sänger, Heiberg, Gade, Guillemain (tuberculosis of the ovaries). Tuberculosis of the ovaries arises through the secondary infiltration of the wall of a proliferating cystoma by tubercles, or through the primary origin of a caseous focus in the ovary itself. We have already referred to the observations upon tuberculous and lupoid disease of the vulva and vagina.

In primary cases, as well as in the secondary, the tube is the favorite seat of disease. Heiberg found tuberculosis of the tubes seven times, of the uterus seven times, and of the ovaries four times.

Tuberculosis of the genitals is, as a rule, associated with tuberculosis of some other organ. Villard found the lungs diseased in one-half of the cases of genital tuberculosis, and in 70 per cent. of the cases which came to autopsy; the urinary apparatus was involved in 56 per cent.

Deschamps found the labia minora almost entirely destroyed by a tuberculous ulcer in a young consumptive of twenty-five, who at the same time presented a tuberculous ulcer of the dorsum of the hand. Very frequently it is derived from disease of the peritoneum, which it may, however, precede.

Attention may here be called to the intimate relationship existing between the genital organs and the peritoneum; this depends especially upon the seminal vesicles, and also upon the tunica vaginalis of the testicle in case of complete or incomplete patency of the processus vaginalis.

English has written upon tuberculous periurethritis in tuberculous individuals, Michaud upon tuberculous ulcerations of the urethra in renal and pulmonary tuberculosis. Ahrens has covered the same topic in connection with tuberculous cavities and pulmonary foci of apparently previous origin, digesting the literature up to 1892.

Tuberculous pyosalpinx, combined with tuberculous peritonitis and phthisis, has been observed by Smith; combined with tuberculous peritonitis alone, by Sänger. The gut is frequently the primary focus.

Brodie found tuberculosis of the peritoneum and of the cavum uteri in a six-year-old child, the gut and omentum being the site of primary disease, the lungs being free. In a case of Chiari's there were ulcerations of the right labia, in addition to large, old tuberculous ulcers of the rectum and posterior margin of the anus. Habershon had a case of tuberculosis of both tubes and ovaries, in which the ovaries communicated with a loop of intestine at the site of an intestinal ulcer. Lichotzky observed tuberculosis of both tubes, and adhesions of the right tube to the ileum. Many authors have attempted to bring genital tuberculosis into some sort of connection with syphilis and gonorrhea. Schuchardt observed tuberculosis of both groups of inguinal glands, subsequent to a soft chancre, in an otherwise healthy man. In a girl he found two flat ulcers at the introitus vaginæ, the secretion containing both gonococci and tubercle bacilli; this was followed by tuberculosis of the inguinal and pelvic glands. This patient had had a cough for some time, and the sputum contained tubercle bacilli, and a man with whom she had had intercourse for more than a year had died eight weeks before of tuberculosis.

Schuchardt regards these cases as somewhat doubtful on account of the possible confusion with smegma bacillus. According to my own experience, however, any such doubt is removed by the multiple foci of caseation and softening in the inguinal glands. In another case a double-sided epididymitis with fistula formation succeeded a gonorrhea, and in still another, in a man who had coughed for some time, a tuberculous process of the prostate succeeded the same disease. Furthermore, Schuchardt was able to demonstrate tubercle bacilli in the gonorrheal secretion of two out of six cases. In these cases, however, confusion with smegma bacilli is not to be excluded, as a spontaneous cure resulted.

Saulmann saw gonorrhea complicated with tuberculous salpingitis in a young, otherwise healthy woman. Fabry saw gonorrhea complicated by lues and tuberculosis of the penis in a man of thirty-five, with hereditary taint.

To trauma, likewise, is ascribed a certain amount of importance as a factor in the development of genital tuberculosis. Lievin saw a testicular tuberculosis, after trauma, upon a syphilitic basis. Weinlechner saw large tuberculous ulcers on the external genitals of a woman, depending upon the same factors. In a rabbit infected with tuberculosis the testicle became tuberculous two months after having been subjected to crushing (Simmonds). English is of the opinion that an epididymitis caused by trauma or by infection ordinarily undergoes suppuration in those of a "tuberculous dyscrasia," and that then tubercle bacilli can frequently be demonstrated. Ladame, Maes, and Jacobsohn also consider trauma as a factor in the production of tuberculous epididymitis, whereas Chevki ascribes to it only a subordinate rôle.

The fact that genital tuberculosis is in the majority of cases located in the internal organs, and that it ordinarily spares, or only subsequently involves, the exernal parts, is a stumbling-block for many authors (Fehling). They are unwilling to regard an external infection as the etiological factor, assuming, as they do, that in this case the external parts ought to be involved, and, indeed, primarily so. They are therefore inclined to derive the tuberculosis of the upper genitals from a perhaps latent focus in the body, or from a primary tuberculosis of the mesenteric glands, by hematogenous infection. This, however, is an error. In the first place, the viability of the natural channels is perfectly demonstrated by the fact that spermatozoa frequently penetrate to the tubes, causing tubal pregnancy. In the second place, it is not at all rare, as pointed out by Hegar, to find pus in the tubes, even though the mucous membranes of the vagina and of the uterus are perfectly intact. If gonococci and streptococci are able to find their way to the deeper portions of the genital tract, it is hard to understand why the same power should not be accorded to the tubercle bacilli, which develop far more slowly. All theoretical considerations, such as are based on the outward direction of the ciliary stream, fall to the ground in face of these facts. In the third place, we find analogous conditions in the digestive and respiratory tracts. Both in man and in animals, whether the infection be accidental or artificial, we find that either the lung or the gut becomes involved, though as a rule the parts previously traversed by the bacilli—the nose, mouth, trachea, esophagus, and stomach—fail to reveal any trace of tuberculosis. In consonance with this fact, we are entitled to believe that tuberculosis of the tubes or of the testes may also arise through exogenous infection, the external parts remaining free. Just as with the systems already mentioned, it would seem that the most external organs of the genito-urinary system, namely, those most exposed to infection, are best fortified. In the male sex a deposition of bacteria seems to be opposed by the urine; in women, the same protection is afforded by the mucous secretion, which by its profuseness and by its chemical characteristics seems to destroy the proliferative capacity of the germ. It is true, indeed, that micro-organisms are found in the vagina, at times even pathogenic germs, but never in such numbers as would indicate proliferation *in situ*. Fresh acquisitions of germs are continually made from without, and are successively destroyed after a longer or shorter sojourn. It has frequently been claimed that the virulence of the bacteria is attenuated, and a corresponding antibacterial power has been ascribed to the secretions of the vagina (Menge, Krönig). According to Will, the acidity of this secretion is inimical to the bacteria. The vagina and the portio are further protected against invasion by their thick squamous epithelium (Hegar, Pozzi), the cervical canal by its well-developed cylindrical epithelium.

Under suitable circumstances, however, as when the germs fasten themselves upon a raw and denuded area, and then work their way into the depths of the tissue, an external infection becomes possible. Of this we cannot entertain any doubt, seeing that a large number of primary affections of this organ have been met.

As regards the male genitals, the cases of circumcision tuberculosis in Jewish children are most notorious in this connection. In the ritual circumcision the anterior portion of the prepuce is cut away, the lamina interna torn with the finger-nail, and the bleeding wound then sucked by the mother (Lindemann). If the operator be luetic or tuberculous, especially if sputum be mingled with the saliva by coughing, there is every chance of a wound infection. Syphilitic infection by this means has already been observed.

In 1893 Lindemann observed two tuberculous ulcers of the penis followed by caseation of the inguinal glands after circumcision by a consumptive. One of these cases ended fatally, the other healed up after a somewhat prolonged course. The mohel himself died two months after performing the said operations.

Lehmann found tuberculous ulcers after ten days, swelling and suppuration of the lumbar glands after three weeks, in ten children who had been ritually circumcised by a consumptive, whereas those children whose blood had been sucked up by another individual remained healthy.

Elsenberg records a similar case, with demonstration of tubercle bacilli in the sputum of the operator, and also in the preputial ulcer of a boy hereditarily untainted; in this case general miliary tuberculosis supervened. The same author met with three identical cases subsequently. Similar observations are recorded by Hofmokl, v. Bergmann, W. Mayer, Eve, Loewenstein, Kolizow (seven cases), Gescheit, Pasternatzki, Chwolsow, Janowitsch, Tschainski.

Baumgarten produced tuberculosis of the urethra experimentally in rabbits, and the author accomplished the same in guinea-pigs (see page 102). Several cases observed by v. Krzywicki also speak for a primary origin.

Kraske has described a tuberculosis of the penis in a man of forty-seven, without association of any of the other organs; he attributed it, however, to a hematogenous infection. Nockher has described a primary tuberculosis of the urethra. Poncet, who had a collection of such cases made by his pupil Barbet, saw a primary tuberculosis of the penis in a youth of eighteen, untainted; the patient denied sexual intercourse. Another patient had a tuberculous infiltration of the urethra.

Malecot found a tuberculous ulcer of the glans in a Jewish boy of fourteen, who had been circumcised. Wickham describes a case of tuberculous ulceration of the penis, stated to be of ten years' standing, in a youth of seventeen, who had previously suffered from Pott's disease. Further, Ssalitscheff described a primary tuberculosis of the glans penis in a man of forty-seven, whose wife had recently fallen sick with cough, laryngitis, and emaciation.

In the female genital tract also a large number of cases of primary and isolated tuberculosis have been described, which would seem to indicate an infection from the exterior. Contributions to this subject have been made by Malthe, Gehle, Predöhl, Kötschau, Schütz, Jacobs, Whitridge, Heiberg, Hünermann, Menge (a girl of twenty, previously scrofulous, with pains in the abdomen six weeks after the first cohabitation, and a nodular tumor after ten weeks), Penrose and Beyea, Frees, Picque, Meinert (virgin of fifteen, with tuberculous salpingitis; extirpation; healthy five years later). The disease ordinarily starts from the tubes. Sippel (case of a virgin of twenty, hereditarily tainted, otherwise healthy, with tuberculosis starting from the cavum; cured two and one-half years after operative procedure). Franqué (two tubercles, size of plums, in a uterus extirpated for cancroid of portio), Jones (probably primary tuberculosis of vagina), Angelini (tuberculosis of vagina and uterus), Friedländer, Veit, Emanuel Kaufmann (primary tuberculosis of cervix), Meyer (tuberculosis of cervix in an individual who had previously had lupus of the face), Bossi (primary tuberculosis of uterus in a woman of twenty-seven, otherwise showing no symptoms of the disease, husband tuberculous; two cases of primary tuberculosis of vulva), Madlehner (primary ovarian tuberculosis, one year after appearance of growth, first symptoms in lungs). Mosler found that 9 out of 46 cases of genital tuberculosis were primary, Spaeth 28 out of 119 cases, both 23.5 per cent.

There is a certain abuse of terms, in that many authors designate cases as primary in which the part involved is the first of the abdominal viscera to be diseased, whereas primarity, in the true sense of the word, denotes the absence of disease in all the other organs of the body at the time of onset of the disease (Sachs). The primarity of genital tuberculosis is vouched for by the fact that it very frequently affects healthy individuals, and also that a timely surgical interference, with radical removal of the part, whether testicle or tube or uterus, is often followed by permanent recovery (*e. g.*, castration—Gibson).

Now and again the infection of the genitals, especially of females, is mediated by fingers soiled with sputum, by clothing, instruments, irrigators, catheters, etc. (Wiedow, Hegar, Whitridge); the most important factor, however, is coitus. This is indicated by the predominance of the disease during the years of maturity, and the not infrequent combination of a tuberculous with a venereal infection.

The assumption of an infection through coitus is coupled with the notion that the female is infected by the sperm of a tuberculous male, or a male by the vaginal secretions of the female. The logical presumption, however, that the spermatic fluid and the vaginal secretion do actually contain the tubercle bacilli, lacks the support of facts. It does, indeed, hold good for the rather small number of cases in which either the genital or the uropoietic system of the original carrier of the disease is the seat of the tuberculous and caseous focus.

Thus, for example, in the cases of five women suffering from genital tuberculosis, Derville was able to show that the husband of every one of them had a tuberculous affection of the epididymis. He failed to determine whether the sperma, also, contained tubercle bacilli. In general, the *libido et potentia cœundi* is diminished in the presence of genital tuberculosis, and the sexual impulse may become entirely suspended. A number of contrary observations, however, have been made by Simmonds, for example, of a patient with tuberculosis of both epididymes and of one seminal vesicle, and of another patient who had submitted to castration on the left side on account of tuberculosis of the testicle, and in whom the right testicle and both seminal vesicles were diseased, both of whom were capable of performing a normal coitus. Similarly, two individuals with unilateral tuberculous orchitis led a normal conjugal life, and produced children, which were still healthy, nine months and two years respectively after birth.

In the overwhelming majority of cases, however, it is not the urogenital organs, but the lungs, which are the seat of the disease. Cases have been reported by Fernet, in which women acquired an apparently primary genital tuberculosis through sexual intercourse with tuberculous individuals in whom the genital organs were not involved. These would seem to indicate that localized disease of these organs is not absolutely essential to the production of infection through coitus. Frankenburger investigated the surroundings of a working-girl who developed a primary tuberculosis of the genital organs, and found that the man with whom she had sexual intercourse showed the remnants of an old left-sided pleurisy. Jani found tubercle bacilli in the healthy testes of men who had died of pulmonary tuberculosis, and this might lead one to suppose that they would also be present in the spermatic fluid. But these conclusions are not above suspicion, for reasons to be given below, in the chapter upon Heredity. Nor are we entitled to draw inferences as to the conditions which exist in human beings from Gärtner's experiments with infected guinea-pigs. He found that semen which was artificially withdrawn from these animals *per frictionem* contained tubercle bacilli, but the notoriously rapid dissemination of the disease in them does not permit of a comparison with man. It has been demonstrated by the investigations of Rohlff and Westermayer that the spermatic fluid of consumptives is, as a rule, free from bacteria. Walther, likewise, could not find a single tubercle bacillus in 272 sections of the testes, epididymes, and prostates of 12 tuberculous individuals, nor was he able to infect animals by inoculation of this material.

Notwithstanding all these facts, coitus may still be the chief factor in the production of genital tuberculosis. The fact was accidentally brought to my notice that many individuals—not only the *venus vulgivaga*, but even those in higher circles—were accustomed to smear the penis or the vulva with saliva, in case the genitals were not well lubricated and the act of coitus produced pain. If, then, the person (man or woman) contributing the saliva be affected with pulmonary consumption, infection of the penis or the vulva may easily be brought about by particles of sputa which happen to be in the mouth. It is a matter of chance whether either one, or which, of the individuals in coitus develops a tuberculosis of the genitals.

Bacilli introduced in this manner may be actually rubbed into the lower genitals by friction, as shown by my animal experiments (see page 102), and find their way into the tissues the more easily because minute epithelial erosions and ulcerations frequently exist.

Indeed, traumatisms of considerable extent are frequently caused by reckless or incorrect coitus; for example, rupture of the vagina with profuse hemorrhage (Barthel), perforation through the recto-vaginal septum (Spaeth), laceration of the posterior vaginal wall to the extent of 5 cm. in a widow of thirty-nine (Polacco), and rupture at the same place (Lyow).. In the same fashion, the epithelial lesions produced by gonorrhea or by syphilis are elements favoring infection.

Or the tubercle bacilli find their way into the deeper parts of the system by the same channels as the gonococci or the spermatozoa; the female genitals are more predisposed than are the male organs to an infection of this character, by reason both of their character and of their anatomical make-up.

In searching for the source of such an infection, it is not sufficient to inquire into the health of the husband or wife, but one must sedulously investigate the entire circle of the sexual acquaintance of the patient, notwithstanding his own denials. Moreover, we must not forget to lay due stress upon masturbation as an indirect factor in the causation of genital tuberculosis.

To give an idea of the extraordinary measures made use of for the latter purpose, I will relate a number of instances discovered by physicians. The casuistics of this subject, however, are very extensive.

For example, Weil withdrew from the male urethra or bladder a goose-quill with feathers; Partsch, a piece of wax-taper; Seydel, a Christmas-tree candle; H. Saratoga, the same object from the bladder of a man of sixty; Neuhaus, a lead-pencil; the author, a hairpin; Görl, a willow switch 34 cm. long, which reached up into the bladder; Samain, a bean out of the bladder of a man of thirty-eight; Morand, three beans. Büchner removed a condom from the bladder of a man who had introduced it for the purpose of preventing conception, not understanding its proper use. Hairpins are very frequent objects in the female genitals, even *in virgino;* thus, Roediger removed one from a girl of seventeen, Cubasch from a female of thirty, etc. Further, pieces of wood, of bone, cigar-stumps, and sealing-wax have been removed by Dittel. Newton removed a small phial; Freund, a packet of needles; Sabolotzky, a "spur" (rubber ring to irritate the female); Winternitz, a roll of feathers which had lain for six years in the vagina of an unmarried woman of twenty-six; Bazzanella removed a goblet (!) weighing 150 grams, and 8 cm. high, introduced by a man into the vagina of his wife in order to preclude sexual intercourse during his absence. Cipinsky removed a caraffe stopper. Stüler took 12 marks in silver, rolled up in a newspaper, from the vagina of a *puella publica.*

All ages are included in the casuistics of this subject; for example, a girl of twelve (Hochmann), or even younger, and a woman of forty-five, who would only admit that the hairpin must have found its way into the vagina as a result of her sliding down in the bed (Henning). A nineteen-year-old girl, with intact hymen, stated that a piece of bone 6 cm. long had slipped into her bladder by accident (Karlin); another girl was entirely at a loss to explain how a hairpin had found its way into the bladder (Currier).

Yet we must remember that it is only the exceptional cases in which such objects slip from the fingers and must be removed by surgical interference. We may thus get an idea how widespread is this practice, especially among females. In this connection, we may mention the female institutes and boarding-schools. Von Guttceit, who has apparently enjoyed a wide experience in this class of cases, especially emphasizes the fact that in these onanistic practices the saliva is very frequently made use of by either sex to lubricate the finger or other implement employed. It cannot, then, be denied that tuberculous saliva or sputum must also be occasionally employed and carried into the deeper parts of the genitals, a mode of infection which, according to the examples above adduced, is excluded neither by youth nor by age, neither by an intact hymen nor by the denials of the subject, as several authors have assumed.

Another piece of collateral evidence of no slight importance is contributed by the instances of extragenital chancre, in so far as these are traceable to sexual perversity, that is, to copulation between the mouth and the genitals. Following are some examples of this: A tonsillary chancre in a man, acquired by unnatural coitus (Knight); a luetic chancre of the lips, acquired by kissing the female genitals (Rona); an anal chancre after pederasty (v. Düring), and many others. Since only a very insignificant portion of these acts produce an infection, we are entitled to infer a rather widespread dissemination of this sexual perversion in certain countries and localities. Moreover, we must admit it to be extremely probable that just as the syphilitic poison can be communicated from the genitals to the mouth, so, on the other hand, the tuberculous virus may be carried from the mouth of a tuberculous individual to the genitals of another. This probability is rather enhanced by the fact that tuberculosis does not stand behind syphilis in the frequency of its occurrence.

Nothing is further from my intentions than to refer all cases of genital tuberculosis to one of the last-mentioned modes of infection, but it is certain that the importance of the sputum, in its character of lubricant and so forth, is greater than of the spermatic fluid, which is, as a rule, germ-free. Indeed, one is justified in assuming that tuberculous infection would be very much more frequent, in a ratio corresponding to the very wide dissemination of the above-described practices, were it not that the saliva of consumptives is, as a rule, free from germs. This we maintain to be the case, in spite of recent assertions of Flügge to the contrary. It is very difficult to establish the etiology of such infections in detail, inasmuch as the physician does not feel the same liberty to inquire into sexual perversions as in syphilis.

Against the exogenous mode of infection one might urge the frequency of genital tuberculosis in very young children, who are not very likely to be exposed to such abuse. Cases of tuberculosis in children are reported by Lannois, Monks, Koplik, Giralde, Comby, Meissner, and Phocas. Among 2760 boys of the ambulatory clinic, Julien found 17 cases of orchitis, of which 5 occurred in children under one year; the majority showed other forms of tuberculous disease. Hutinel and Deschamps, who observed 9 cases in one and one-fourth years, assert that as a rule the hereditary factor is absolutely lacking; disease of the intestines or of the peritoneum had generally gone before. Among 51 cases of testicular tuberculosis in individuals under seventeen (Kantorowicz), one-half were found to be composed of children under three years of age.

Tuberculous disease of the mucous membrane of the vulva and the vagina has been observed by Demme in small girls, one of them as young as thirteen months, the mother of whom was phthisical. Morton found extensive genital tuberculosis in a phthisical girl of eight.

Although dissemination of the tuberculous virus is of the hematogenous type in children, as also in guinea-pigs, far more frequently than in adults, there is yet no sound reason for assuming that this infantile genital tuberculosis is necessarily secondary to a previously developed, perhaps congenital focus. The gonorrheal genital affections in earlier and later childhood are analogous in their nature, yet no one dreams of ascribing to these a congenital or hematogenous origin, since all the facts point to an exogenous infection.

I refer here to the observations of E. Fränkel, Dusch, Epstein, Prochownick, and others. Wydmark records 8 cases of vulvovaginitis gonorrheica in small girls. One of these occurred in a girl of two and one-half years, whose mother had been infected with gonorrhea by her husband, and then made use of the same cloth to clean her own genitals and those of the child. Another case occurred in a girl of nine, whose eight-year-old brother was soon after taken sick with urethritis of the gonorrheal type (gonococci). Still another was in a girl of six, who had played "marrying" with a boy of thirteen. Cahen-Brach within a short space of time met with 25 cases of gonorrheic vulvovaginitis in girls of from one and one-half to twelve years, of whom 19 were under seven. In seven cases stuprum was admitted; in the others the infection was traceable to sleeping with the mother or some other person, to the use of infected towels, etc. Cassel found gonococci in twenty-four out of thirty girls who had a purulent genital discharge; in one of these the infection was traceable to stuprum with a brother of eighteen, having gonorrhea; in ten cases the source of infection was not ascertainable; in others it was supplied by the diseased father or other housemate, sleeping-companion, etc.

The etiology of these gonorrheal affections throws considerable light upon the origin of tuberculous disease of the genital organs in children, since the analogy between the two cannot be disputed.

Two autopsy findings in the experience of the author may be here recorded. A girl one year of age with pulmonary phthisis presented a spina ventosa of the digits and a caseous ulcer of the clitoris. Another girl of the same age presented, in addition to pulmonary tuberculosis, hypertrophied phalangeal joints with secreting sinuses and flat ulcers with caseous bases upon a hypertrophic clitoris extending over to the labia. May we not regard the discharging finger as an agent in the production of the genital tuberculosis, and may not the normal finger in still other cases mediate the infection between tuberculous areas and the genital organs? It is well known that even very small children practice onanism, either of their own initiative or through the influence of evil surroundings.

Spaeth lays great stress upon the barrier which is opposed to the progress of the gonococci, and indeed of all infectious germs, by the firmly closed external os of nulliparæ. It is, indeed, true that the internal genitals and the peritoneum are in great measure shielded from invasion by this means, yet our case-records of peritonitis in small children, subsequent to gonorrheal infections, demonstrate that this obstruction is not in all cases impassable. Such cases are reported by Leven, Sänger, Welander, and others, and some of them have resulted fatally.

In addition to the exogenous mode of infection, tuberculous disease of the genitals may be derived from neighboring foci, may occur by lymphoid infection (especially from the peritoneum), may travel in rare cases along the uropoietic system, or also along the vascular channels.

From all this it is evident that an exogenous autoinfection of the external and internal genitals may be brought about in consumptives of either sex by the sputum. An intercurrent genital tuberculosis in a consumptive is therefore not necessarily attributable to a hematogenous or lymphogenic infection. In case the organs which lie between the lungs and genitals are free and intact, this mode of infection is not even to be regarded as probable. In doubtful cases the autopsical findings are decisive, inasmuch as the occurrence of multiple miliary nodules in similar stages of development points to a blood infection, while the occurrence of single foci of large size, alone or in association with others, points to an exogenous source.

The attempts to explain the varying ages of the foci upon the basis of a series of recurrent infections along the blood-channels is inadmissible, since it is altogether too improbable that the bacilli thus discharged into the blood-stream should always find their way into the same organ and to the same areas, notwithstanding the fact that so many other parts and organs are open to them.

Infection of the Uropoietic System.—At the very opening of this chapter it was explained that tuberculosis of the urinary apparatus was, as a rule, to be regarded as secondary to, and dependent upon, a genital tuberculosis, and that the course of infection was rarely of a reversed type. The causes of infection are, however, similar in kind, namely, instruments, catheters, bougies, coitus, masturbating, etc. If, now, we follow the *materies morbi*, the bacillus, in its progress from the exterior inward, from the genital focus to the urinary system, the difference between the two sexes strikes us very forcibly.

The tubercle bacillus which finds its way into the male urethra, whether in the same manner as the gonococcus or by the mediation of some foreign body, has very little chance of gaining a firm footing. Unless erosions happen to be present, it is most likely to be washed out again by the frequent urinations. The prostatic portion, in which the mucosa is bored like a sieve, affords the first asylum and the first chance for colonization. Thus it is often the point of departure of a tuberculous infection both for the urinary and the genital apparatus. It is, as it were, the crossways of both systems, yet the bacteria tend to settle by preference in the genital channels, as is shown by the greater frequency of disease in those parts. This is, of course, partly explained by the fact that they are in less danger of being swept out again by the passing secretions.

The invasion of the bladder by the bacilli is probably no rare occurrence, but the abundance of the urine is unfavorable to their deposition and washes them out again in the majority of cases.

The same conditions maintain in the female genitals, except that here the shortness of the urethra is still less favorable for the development of the bacilli. Ahrens could find only four cases in the literature up to 1892. On the other hand, the bladder is far more open, and would seem to be better exposed to a direct invasion of the bacilli than in the male, whether this proceeds from the exterior or from a deep-lying focus in the genital tract. In this connection I may remind the reader that coitus has occasionally been carried on directly into the bladder, and that a large number of foreign bodies have been extracted therefrom.

In a case of tuberculosis of the kidney, traceable in all probability to the bladder, the eighteen-year-old patient admitted coitus with a tuberculous individual as a possible cause of the vesical trouble (Finne).

Vesical tuberculosis in the woman is less frequent than in the man. This is not improbably due to the fact that tuberculosis of the prostate is ordinarily an antecedent condition, and that the bladder is thence subject to frequent invasions of the bacilli.

As was stated in the introductory paragraphs, bacilli may find their way from the bladder to the kidneys. Just as ascent of a catarrhal inflammation (pyelonephritis) through the ureters to the pelvis is not at all rare, so, too, the tubercle bacillus may find its way from below upward (Aby). Since, however, only a few bacilli can be involved, and since these reach only certain limited areas, the foci become localized at first especially upon the mucosa of the calices and of the papillæ. Only as the disease progresses do they extend over to the actual parenchyma of the kidney, and lead to diffuse, communicating foci and widespread destruction (nephrophthisis). In childhood, in which an external infection is much less apt to occur, nephrophthisis is far rarer.

According to most authors, men are more often diseased than women. Eichhorst, however, had 16 men and 22 women among 38 cases of tuberculosis of the kidneys, notwithstanding the fact that the total number of female patients was considerably smaller than the male.

The actual urinary passages, the urethra and the ureters, are less exposed to the deposition of bacteria than are the bladder and the pelvis of the kidney. As has been previously explained, the constant play of urine through the ureters, and its forcible passage through the urethra, are very efficient means of removing the infection. In the pelvis and the bladder there is some degree of stagnation; the trigonum and the opening of the ureters are the sites of least resistance in the bladder. Disease of the kidneys may occur in combination with a normal bladder, nor does this condition necessarily exclude an infection from without. We need only recall the analogous infections of the deeper parts of the respiratory and intestinal tracts, in which the upper passages are not involved.

The invasion and settlement of bacteria in the urinary passages is favored by the existence of gonorrhea, of strictures and phimosis, of previous nephritis, and of trauma (Duret). Salzmann found a tuberculosis of the anterior urethra and of the glans in a young man with a phimosis and an old stricture behind the fossa navalis. Some writers (Jaccoud) believe that repeated congestions, or alcoholism, favor the invasion of the bacteria. Gravidity, also, is believed to have an unfavorable influence upon the tuberculosis, perhaps on account of the acceleration of the lymph-stream from Douglas's space, in which the tubercle bacilli are more likely to assemble (Sommer).

Finally, we may mention the occurrence of a hematogenous tuberculous nephritis, with formation of multiple large and small nodules. This is a complication which accompanies general miliary tuberculosis with comparative frequency. It is a mode of infection which is less of clinical than of pathological interest, as in the other organs which become so diseased. Von Krzywicki had not a single case which indicated hematogenous infection among 29 which came under his notice.

I have made the assumption in the above discussion that tubercle bacilli may be taken up into the body at any point of the periphery, lung, gut, or surface lesion; that they may not elicit any pathological changes in these resistant organs; that they may then find their way into the blood-stream; and that, finally, in being eliminated by the kidneys, they may effect a settlement in these rather susceptible organs (Stintzing) of the body. The assumption is, however, theoretical rather than based upon the actual demonstrations of fact.

INFECTION OF THE EYE.

The first observations of tuberculosis in the eye were made by Autenrieth (1808), Guéneau de Mussy (1837), and Gerlach (1852). In these cases the choroid was involved. Following upon the discovery of the ophthalmoscope, more accurate descriptions were furnished by Jäger, Manz, Busch. Simultaneously with Jäger, v. Graefe described a choroiditis in the eye of a boy. Previous observations established the connection between choroidal tuberculosis and tuberculosis of the lungs and meninges. Cohnheim in 1867 regarded it as the expression of a generalized tuberculosis, especially of the acute miliary type, and employed the ophthalmoscope in the diagnosis of that disease. And although the expectations so aroused were not completely justified, yet his suggestion brought a number of valuable accessions to medicine (S. Weiss, B. Fränkel, Money).

Tuberculosis of the iris, occurring bilaterally, was first described by Gradenigo (1869), Perls (1873), and Caspary. Köster found isolated miliary tubercles in a granuloma of the iris, the other organs of the body being sound. According to Manfredi, the iridal affections of the older authors comprise mainly tuberculous processes, a suggestion which is backed also by Haensell, Haab, and others. The knowledge of tuberculosis of the iris became more firmly established by the casuistical contributions of Manfredi, Weiss, Samelsohn, Sattler, Haensell, Haab, Falchy, Rüter, v. Arlt, Wolff, Maren, and others. The other parts of the eye only rarely become the seat of tuberculous processes. Tubercles in the retina were first seen by Bouchut, Perls, Manfredi, and Weiss.

Tuberculosis of the optic nerves and of their sheaths, and of the retina, were described by Sattler, who referred to similar observations by Cruveilhier and Hjort. Von Herff described 15 such cases in the literature.

Tubercles in the vitreous were described by Poncet, Falchi, Eperon, and Haensell; they were all secondarily acquired. Deutschmann found a hyaline, refractory mass, of tuberculous nature, in the center of the vitreous of an enucleated human eye, and interpreted it as a primary tuberculosis of the vitreous.

In a case of Köhler's, cited by Wagenmann, the sclera was the primary seat of the tuberculous process. Ordinarily the sclera is involved in the tuberculous process only through perforation.

The cornea, too, seems to become diseased chiefly through perforation from the deeper parts, or through simultaneous conjunctival tuberculosis. Arcoleo claimed to be the first to observe primary tubercles of the cornea. Later on, similar instances were described by Sattler, Panas and Vassaux, Nikati, Roy and Alvarez.

A short communication of Köster's contained the first intimation that the conjunctiva was also subject to tuberculosis. More detailed studies were subsequently contributed by Sattler, Walb, Herter, Bock, Baumgarten, Amiet, Burnett, Denig, and others. The lupoid form of conjunctival tuberculosis was observed by Alexander Pflüger and Hans Adler; it was made the object of careful histological investigation by Neumann and Laskiewicz, and casuistically enriched by the contributions of Horner, Milligan, Falchi, and many others.

As regards the frequency of ocular tuberculosis, Rokitansky asserts that in 14,000 cases he had never seen it, Hirschberg that in 60,000 eye-patients he had seen it only 12 times, whereas Mules in Manchester saw it once in 33,000 cases. These figures date in part from a time at which the correct appreciation of the disease was just making its way. As knowledge of the disease became more accurate, observations likewise became more frequent, as can best be seen in connection with tuberculosis of the conjunctiva. Köster contributed the first case in 1873, in 1879 Haab collected 7 such cases, and in 1887 Amiet could point to 47 recorded cases. Even at the present time it is not unlikely that many cases of ocular tuberculosis pass under another name. In animals I was not always able to determine such typical changes as are described in the symptomatology, and the human disease also undoubtedly occasionally lacks these characteristics. Vignes, therefore, considers it of diagnostic importance that every piece of ulcerated tissue shall be microscopically examined, and not the pus alone examined. Parinaud found that in some cases the tuberculous character of the disease could be established only by inoculation experiments. It is very possible that the typical anatomical picture in superficial foci may be essentially altered by secondary infections.

Sattler found a large number of miliary tubercles in a glioma of the retina, and Valude refers to the researches of da Gama Pinto concerning the intimate relationship between glioma and tuberculosis of the eye. H. Wagner characterizes the chalazion as partially tuberculous granulation tissue; Tangl found tubercle bacilli in a considerable number of these structures, as have also several other authors, but their conclusions must be accepted with a certain amount of reserve, since, in view of the absence of inoculation experiments, one cannot positively exclude the smegma bacillus. The conception of chalazia as tuberculous structures has been opposed by Weiss, Deutschmann, Landwehr, and Deyl.

If we review the clinical and experimental data, we are brought to the conclusion that no portion of the eye is immune against the tubercle bacillus. Wherever it finds a resting-place, it meets with the conditions necessary for its further growth, whether in the choroid, the cornea, the vitreous, the connective tissue, or even the lachrymal sac.

The tuberculous diseases of the eye are of two kinds, according as they involve the anterior or the posterior portion of the organ. This subdivision is justified both by the symptomatology, by the prognosis, and by the course.

Disseminated tuberculosis of the choroid, as was shown by Cohnheim, is usually the expression of a general infection, and therefore only a symptom of acute miliary tuberculosis. So, too, Bock found that 19 out of 23 bulbi, in 15 autopsies on cases of acute general miliary tuberculosis, showed tuberculosis of the choroid. Simultaneously with the choroid, the meninges or the brain may also be involved. In a case of Hirschberg's there was a tuberculous tumor in the pons. The participation of the choroid in cases in which the blood contains the bacilli, namely, acute miliary tuberculosis, is probably due to the rich vascularization of this tissue.

Whereas in the choroid the disease is generally bilateral, in the anterior portion of the bulb and in the external parts, the conjunctiva, tear-ducts, and lids it generally occurs only on one side, so that we may assume the infection to have taken place otherwise than through the blood-stream. The iris appears to be the most frequent site of tubercle formation.

Tuberculosis of the iris may arise secondarily, either by continuous extension or by metastasis (especially from the lung), but it may also be the primary focus in the body. Poncet presented a boy of sixteen, hereditarily untainted and in good health, who exhibited a primary tuberculosis of the iris. The eye was enucleated, and the boy did not subsequently show any symptoms of tuberculosis. Schäfer details another case of primary tuberculosis of the uveal tract in a soldier who was healthy and of good antecedents (hypopyon and external perforation).

Wagenmann observed a case of iridocyclitis tuberculosa in a man of forty-four, who was hereditarily untainted and showed no other symptoms of tuberculous disease. Jan Hoene records a case of primary iris tuberculosis in a soldier of twenty-two, otherwise healthy. Neese found a tuberculous granuloma at the boundary between the choroid and corpus ciliare; after the enucleation no further symptoms of tuberculous infection developed.

Occasionally the environment of the patient supplies the etiology for the infection. Thus Swanzy describes the case of a child of two, otherwise healthy, who had a tuberculous nodule of the iris, which impinged on the posterior surface of the cornea. The parents of the child were phthisical. The child remained healthy five months after extirpation of the eye.

The position of the anterior chamber renders an infection from without extremely improbable, unless the bulb be perforated. Yet the possibility of such an occurrence cannot be absolutely excluded, especially when we consider that the conjunctiva, the various mucosæ, and even the outer skin (see page 100) have been shown to be viable for the tubercle bacillus.

As an example of how foreign bodies can find their way even as far as the iris, without the aid of any degree of violence, we may cite a case of Pagenstecher's. He found nodules upon the surface of the conjunctiva, bulb, cornea, and iris of an eye into which a caterpillar had fallen. The nodules were not tuberculous, and in the center of each of them a caterpillar hair could be demonstrated.

Treitel saw a tumor as large as a pea in the iris, and a keratoiritis, in a boy of twelve, healthy and of good antecedents, following upon an injury with a straw four months previously. The nodules appeared three weeks after the injury, which corresponds to the period of incubation after inoculation.

A case of Wolfe illustrates the rare occurrence of an infection through a trauma. A boy of eight, in good health, received a blow upon the left eye; swelling ensued and in about a month a tuberculous growth in the anterior chamber upon the upper margin of the iris.

If the cornea and the conjunctiva are primarily diseased, the assumption of an external infection is probable, and is rendered even more plausible by the contrasting conditions in tuberculosis of the choroid. In case of the latter there are, as a rule, multiple foci in the body or tuberculosis of neighboring areas, bilateral occurrence, poor prognosis, and death. On the other hand, in tuberculosis of the conjunctiva and cornea there are no multiple foci, the disease is monocular, the prognosis after early removal of the focus is favorable, and recovery is often complete.

In individuals with some other secretory tuberculous focus, especially in consumptives with abundant expectoration, opportunity to infect the eye with the finger or otherwise is of course abundantly afforded.

Thus, we find conjunctival tuberculosis not infrequently combined with an antecedent pulmonary tuberculosis, as in the cases of Herter, Wagenmann, Gerin-Roze, Rampoldi, and Hock. Or there may be other external tuberculous foci—Stölting observed a case of conjunctival tuberculosis in a girl of twenty, otherwise healthy, who had previously suffered for a considerable time with a tuberculous ulcer of the cheek. E. Bock records the case of a girl who presented simultaneously tuberculosis of the tear-sac and tuberculous fistulæ of the right elbow, and remarks that she had evidently carried the pus into her right eye by means of the fingers of the left hand, with which she cleansed and bandaged the right elbow.

In other cases a lupus may supply the original material for an infection of the eye. For example, there was a nasal lupus in cases of Csapodi and Wagenmann, a lupoid ulcer of the neck and of the external commissure of the eye in cases of Hill Griffith and of Little, lupus of the alæ nasæ in a case of Knapp, and lupus of various parts of the face in four cases contributed by Luc.

In certain of these cases a lupoid or tuberculous affection of the connective tissue afforded a continuous extension of the primary lupus; in others the lupus was isolated and the infection was evidently secondarily brought about by the fingers; while in a third set of cases the primary tuberculosis of the eye extended by continuity over to the cheek. Thus, in advanced cases it is often difficult to determine where the disease had its primary location, as in a case of Laskiewicz (lupus of the conjunctiva and cornea in a boy of fourteen, with simultaneous lupus of the nose). And yet there are a considerable number of cases on record in which no other form of tuberculosis had gone before, and in which the disease of the conjunctiva or of the cornea constituted the primary focus. Cases of this character have been described by Arlt, Gavet, Köster, Leidholdt, Parinaud, Peck, Walb, etc.

Now and again we are enabled to trace not only the source, but also the mode of infection. Thus Löwenthal describes the case of a healthy woman who shared her bed with a phthisical husband, and was accustomed to lie with her left side turned toward him; she developed tuberculosis of the conjunctiva of the left eye. Pregel had under his care a young woman of eighteen, with tuberculosis of the left lower lid, who had first produced an inflammation of the eye by introducing various foreign bodies, and had then had it licked out, a method of cure much in vogue among the laity. Pflüger observed a girl of twenty, an orphan, with lupus of the conjunctiva. This girl had lived for fifteen years with her godmother, who was afflicted with a destructive ulcerative process of the nose. As the girl had lived in the same room and had slept in the same bed, the godmother was of the opinion that the child had acquired the disease from her.

Two sisters with tuberculosis of the conjunctiva came to Rhein, and he was convinced from the circumstances of the case that the elder, a girl of twenty, had received the infection from the younger, who had had the same trouble for a considerable time previously. Both parents and four sisters of these girls were alive and in good health.

The source of infection of ocular tuberculosis has hitherto rarely been demonstrated, since physicians have satisfied themselves with the assumption of an hereditary taint, and have ignored the possibility of an infection.

Accidental traumatisms favor infection. A child of one and one-half years wounded its left eye by falling upon a sharp edge; this was followed by recovery, with a subsequent secondary swelling of the upper lid; after eight weeks tuberculous granulations of the conjunctiva.

A case of Fano's indicates the possibility of infection during operation. A girl of thirteen was operated on for strabismus, and ligatures were introduced, which healed well. In two months a grayish tuberculous nodule developed at the upper and inner border of the bulbus, and grew in size, so that after another month enucleation had to be performed.

The monocular occurrence of conjunctival and corneal tuberculosis, which, as has been previously stated, is characteristic of an exogenous infection, has been established by numerous observations, and has been especially emphasized by Amiet in his statistical résumé. If both eyes are affected, as in the two cases of Baumgarten, in the case of Csapodi, of Haab, and of Stölting, it is usually apparent from the diverse appearance of the two sides that one of them is more recent than the other, and has in all probability received its infection therefrom. The habit which many individuals have of fiddling with their eyes and their nose affords ample opportunity for such autoinfection. The other alternative, namely, that tubercle bacilli in the blood-stream upon successive occasions select the eye exclusively as their nidus for development, certainly seems forced. Further, the transmigration of the infection from one eye to the other along the lymph-channels does not seem a factor of any consequence, in view of the very slight tendency of an anterior focus to infect the posterior parts of the eye. The lack of any relationship between conjunctival or corneal tuberculosis and internal disease may also be argued from the very favorable prognosis of these conditions after early operations, a prognosis which could hardly be justified if they were due to the presence of bacilli in the circulating blood. A timely and radical removal of the new tissue is often synonymous with an arrest of the process and complete recovery, as is shown by the observations of Falchi, Pflüger, Stölting, and others.

The case of corneal tuberculosis recorded by Panas goes to show that even if the process is left to itself it may undergo retrogressive changes.

In tuberculous affections of the conjunctiva, cornea, and iris (Haab), the preauricular, maxillary, and cervical glands are sympathetically affected, either exclusively or chiefly, upon the same side.

Many authors have been inclined to regard the matter from the standpoint of the older conception, according to which the scrofulous glands were the expression of a diathesis, upon the basis of which the ocular affections were only secondarily developed.

As late as 1886 Wagenmann regarded the occurrence of primary tuberculosis of the eye as improbable.

Granting that the glands may simultaneously become affected from some other source, and that the disease of the eye may represent a fresh and independent focus of infection, yet the drainage-area of the periauricular and of the preauricular glands is very closely circumscribed, and we shall not go far astray if we interpret a simultaneous inflammation in them in the light of a secondary infection derived from and dependent upon the disease of the eyes.

In this connection a case of Stölting's is of interest, in which the entire lymphoid apparatus of both sides of the neck was infected, and partially broken down (open fistula), as the result of some other source of infection, while the preauricular glands showed swelling only upon the right side, corresponding to a tuberculous conjunctivitis of the right eye.

Under certain circumstances it is possible for the tuberculosis of the glands to become evident clinically before the local affection at the site of invasion gives any symptoms. Thus, for example, in an infection of the conjunctiva a very large proportion of the bacilli may find their way direct to the glands,* while only a very small number remains behind in the original focus. Such an occurrence is especially facilitated by the permeability of the mucous membranes in the young.

It will perhaps seem extraordinary that an organ apparently so exposed as the eye should show so small a proportion of tuberculous infections. Neglecting for the moment the blood as a source of infection, it cannot be denied that tubercle bacilli must occasionally find their way to the cornea and the conjunctiva from external sources. In infected rooms, especially in those inhabited by consumptives, the tubercle bacillus is carried into the eye along with the minutest particles of dust, or conveyed by foreign bodies of large size which are accidentally or purposely introduced into that organ; or, more rarely, it may even be directly coughed into the eye, or carried by a kiss. But the sensitiveness of the eye for foreign bodies and the readiness with which it acts to remove them serve to protect it against the settlement of the tubercle bacillus. A bacillus measuring 0.001 mm. sets up an energetic secretion of tears and a pronounced activity of the palpebræ, whereby it is carried into the angles, washed away, and eliminated. If the bacillus is attached to some larger body, the secretion is reflexly increased. This purely mechanical factor is of great service in preventing the deposition of foreign bodies under a certain size, unless they chance to hook themselves into the folds of the mucous membrane or become forced into it by violent rubbing. In conjunction with the well-developed squamous epithelium, it suffices ordinarily to prevent the settlement of the bacteria. The chemical nature of the lachrymal secretion, which Valude in his fine work upon ocular tuberculosis considers of great moment in restricting the growth of the bacteria, seems of less importance, in view of the fact that a large number of cases of tuberculosis of the lachrymal duct and sac have been recorded. Upon tuberculosis of the sac, we may refer to Haab (Case 1), Ludwig, Stölting, Leithold, Bock; upon tuberculosis of the ducts, to F. Salzer, Baas and Gonella, L. Müller, Süsskind. Catarrhs and other diseases (eczemas) have a varying effect upon the infection. On the one hand, the diseased, swollen, and undermined tissue may facilitate the deposition and invasion of the bacteria. On the other hand, the increased lachrymal secretion and suppuration favor their elimination. The end-result depends upon the comparative value of these two factors.

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* These glands are perhaps of great diagnostic value, since in doubtful cases one would undertake their removal for examination rather than operate upon the eye itself.

The small number of cases of corneal as compared with conjunctival tuberculosis is explained in part by the smaller exposure of surface, in part by its polished character. Thus, foreign bodies, unless driven in with a fair degree of violence, do not remain but are carried into the folds and the fornix of the conjunctiva palpebrarum, where we ordinarily discover the initial tuberculous focus. The structure of the cornea does not exclude the growth of bacteria. It participates in the disease both in cases in which there is a rupture of a posterior focus through the iris, and, as in a case of Stölting's, in cases in which it comes into contact with a tuberculous area in the conjunctiva.

INFECTION OF THE GLANDS.

Our knowledge of glandular tuberculosis has been very much enlarged by animal experiment. If we inoculate animals with tubercle bacilli, into any tissue except the blood, they may do one of two things: Either they settle at the site of inoculation, and find their way only late and in part to the proximal set of glands; or they pass the site of injection and leave behind no trace of their passage. They then are arrested by the proximal set of lymph-glands, the filtrative capacity of which has been emphasized by numerous writers. Here they form colonies and multiply, and eventually, when a caseous focus has developed, they pass on to a second, more distant barrier. The gland itself has ordinarily become considerably enlarged within three to six weeks after the infection. It shows a medullary infiltration, with numbers of fairly large, cheesy foci, which may be softened in the center. Or it may be completely metamorphosed into a thick-walled sac containing a milky, inspissated fluid. It may happen, though rarely, that the gland is hardly larger than normal, so that it becomes evident only upon very close inspection; yet it contains a minute caseous focus, perhaps no larger than half a pin's head in size. Such a focus may be situated in the interior of the gland or in the peripheral parenchyma. Even so small a focus may become the point of departure of a general miliary tuberculosis, as I once observed in an animal after a subcutaneous injection. Dissemination from the primary gland takes not only a centripetal, but also a radial direction, in such wise that the main movement sets in toward the heart, along with the lymph-current; that minor movements take a course vertical to that of the lymph-current; and, finally, that there is a slight tendency, often imperceptible or even lacking, to spread in a direction opposed to that of the lymph-current.

It is often possible to follow this gradual advance, inasmuch as the glandular system exhibits a chain of organs progressively diminishing in size, the cross-sections of which illustrate very neatly the successive stages of the process of infection.

In the same manner, when an infection has occurred upon one side of the body, either in the inguinal region, or in the ear, or in the eye, the glands of the opposite side ordinarily become implicated, even if only to a slight degree.

The inoculation of guinea-pigs with tubercle bacilli affords a means of studying the lymph-glands and their communications. In themselves the glands constitute a fairly reliable filter for the tubercle bacilli, and become incompetent only in the face of successive inundations or of secondary infections, traumata, etc. They then become the media for further infection, the process tending to spread ever inward to the interior of the body, and the opposite side. Here, too, the progressive nature of the advance, the gradual fading out of the process as it is traced centrifugally, becomes plainly evident. In my inoculations tests upon more than 3000 animals, in which these relations are far better manifested than in human beings, I was often driven to ask myself whether too vast a rôle is not assigned to the blood-channels in the dissemination of tuberculous processes, and whether, in reality, the lymphatic system is not far more of a factor in the disease. For example, if we start an infection in the toe of one foot, we find after a time that the popliteal, inguinal, and retroperitoneal glands have become caseous, that the liver and spleen have become tuberculous, and, last of all, that the lungs have yielded and the bronchial glands become caseous. Why, then, if the virus has traveled along the vascular channels, does the pulmonary infection occur so late? And, in reversed circumstances, when we produce an infection within the territory of the cervical glands,—*e. g.*, in the nose,—why do we first get a caseation of these glands and a tuberculosis of the lungs and bronchial glands, and why after a much longer interval an infection of the liver and spleen? The hypothesis of a varying predisposition on the part of the several organs does not help us out of the difficulty, since the same organ which at one time seems the more susceptible, under another set of conditions seems the less so.

Whereas the true blood-infections—*e. g.*, anthrax—are characterized by the infection of glands widely removed from the original site of inoculation, in tuberculosis only the glands proximal to the portal of entry are at first invaded, and from this site progressively onward.

Lymphatic tuberculosis is not for us, as it was for our predecessors, the localized expression of a constitutional anomaly, of a diathesis, but the visible evidence of an infection with tubercle bacilli. We should therefore invariably regard the drainage area of the glands earliest invaded as the site of invasion of the virus, excepting only those rare cases in which there is a centrifugal progression of the disease.

In all species of exogenous infection, no matter in what part of the body they occur, the bacilli must either make a settlement at the point of invasion, or they must wander farther onward. Thus they may constitute a well-limited focus without involving the lymphatic glands, as most frequently in cutaneous infections such as lupus; or, again, they may sooner or later invade the glands, and there go through their full cycle of development. In the latter case the causal relationship between the two infections is easily demonstrated. Finally, the bacilli may pass the external barriers without leaving any trace, and may develop primarily in the glands. The manner of origin of such diseases of the gland, in cases in which there was no evidence of tuberculous change or of other lesions in any part of their drainage territory, was for a long time very obscure. The difficulty was solved by the discovery that skin and mucous membrane, even though macroscopically intact, might permit of the passage of bacteria (see page 100). The existence of a primary glandular tuberculosis, which had for a long time been disputed, was thus established, and also the mode of origin of that form of scrofula which manifested itself as a cervical adenitis.

While glandular tuberculosis is of less importance in adult life, the rôle which it plays in childhood is very great. Wohlgemuth found that 297 out of 4900 children under ten, or 60 per cent., were afflicted with this disease. There was a great predominance of females. Of 82 cases of Garré,* the age distribution was as follows:

From 0 to 9 years	12.2 per cent.
" 10 to 19 "	39.0 "
" 20 to 29 "	28.0 "
" 30 to 39 "	14.6 "
Over 40 years	6.2 "

In 430 cases Wohlgemuth found the distribution to be as follows:

Up to the age of 1	54 cases	= 12.50 per cent.
From 1 to 3 years	104 "	= 24.15 "
" 3 to 5 "	46 "	= 10.70 "
" 5 to 10 "	90 "	= 20.80 "
For the first ten years		68.15 per cent.
From 10 to 20 years	80 cases	= 20.00 per cent.
" 20 years on	50 "	= 11.85 "
		100.00 per cent.

There is a general consensus of opinion that the greatest number of cases are found between birth and the tenth year. According to Th. Bruhn, the female sex has the preponderance of cases, constituting 70 per cent., whereas Wohlgemuth found a proportion of 223 females to 207 males.

The difference between youth and maturity is easily explained. In youth the tubercle bacilli have less difficulty in traversing the mucous membranes, and are first arrested by the glandular barrier. In mature individuals, however, the mucous membranes themselves constitute an efficient barrier, so that the bacilli find their way to the gland only after they have overgrown the peripheral resistance. The preponderance of female cases depends upon the same factors and not upon a "diminished power of resistance," or upon "unfavorable conditions of living," or upon an "increased susceptibility."

In considering the etiology of glandular tuberculosis, we must not neglect any of those factors which we have mentioned in the discussion of the several organs, of the external skin and of the mucous membranes, as conditions predisposing to infection. Herein are included all traumata, especially those of light character, rather than such as are associated with much hemorrhage, lesions of the epithelium, eczemas, burns, foreign bodies, etc.

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* Two-thirds of the patients were females.

Concerning the significance of glandular tuberculosis in general, and the frequency with which the various sets become involved, we may refer to the following statistics.

In the Children's Hospital in Budapest, Bâbes found that more than half of the autopsies performed during the course of eight years revealed the presence of tuberculosis of the lymph-glands, especially of those of the mediastinum and of the bronchi.

Müller found glandular tuberculosis in 126 out of 500 autopsies, ages up to 5 years.

Neumann, in 142 autopsies (up to 15 years), found tuberculosis of the bronchial glands 46 times, these being the ones chiefly noted.

Of the autopsies of children dead of tuberculosis: Steiner and Neureutter found tuberculosis of the lymph-glands in 299 out of 302 cases, the bronchial glands being involved 286 times; Rilliet and Barthez found tuberculosis of the lymphatic glands in 248 cases out of 312 tuberculous bodies; Northrup found the bronchial glands caseous in every one of 125 autopsies held upon tuberculous children in the Foundlings' Home.

Clinical observations yield the following data:

Beruti, lateral cervical glands	88.2	per cent.
Balmann, lateral cervical glands	81.0	"
Balmann, axillary glands	6.0	"
Balmann, inguinal glands	7.0	"
Balmann, cubital glands	5.0	"
Balmann, popliteal glands	0.07	"

Volkmann gives a similar series. The cervical glands are by far the most susceptible to disease, then the cubital, more rarely the axillary, and most rarely those of the fossa poplitea and of the inguinal region. It is, indeed, very rare to find tuberculosis of the inguinal glands in connection with tuberculosis of the bones and joints of the foot, even though the latter attain great severity. On the other hand, they become swollen in tuberculosis of the vulva, vagina, or portio (Zweigbaum).

In 430 cases analyzed by Wohlgemuth, the distribution was as follows:

Cervical glands	93.00	per cent.
Axillary glands	2.78	"
Inguinal glands	0.93	"
Cubital glands	0.23	"
Popliteal glands	0.23	"
Preauricular and postauricular glands	2.90	"

The last four categories presented isolated conditions, in which no peripheral tuberculous process was demonstrable.

Tuberculosis of the cervical glands is preëminent, therefore, among the symptoms, and may justly be called, in the words of v. Bergmann, "the true sign of scrofula." In this regard it stands second only to the bronchial glands. The various glands of the neck, auricular, cervical, and submaxillary, as well as the glands of the supraclavicular and infraclavicular regions, constitute the reservoirs of the lymph-vessels of the organs of the head, of the skin, the eyes, ears, nose, mouth, throat, palate, and tonsils. In conformity with our previous conclusions concerning age and localization, we frequently find that glandular tuberculosis in youth is primary. We are unable to determine accurately the site of invasion of the bacteria, although we may, perhaps, surmise it from the existence of an eczema, of a lupus, etc. In such cases only a small number of bacilli have found their way to the internal tissues. In addition to these latter cases we find glandular tuberculosis not infrequently associated with evident peripheral foci, situated, for example, on the tongue, the gums, the pharynx, the palate, and last, but not least, the tonsils (Abraham, Krückmann, Sacaze). These secondary glandular infections occur less frequently as age advances, so far as our present data permit us to judge. In part their development depends upon the extent of the primary focus, so that if the latter be considerable, they are rarely absent.

Taking as an illustration tuberculosis of the conjunctiva, cornea, or iris (Haab), the lymph-glands which at first become involved are those in the region of the ear, the jaw, and the neck, and predominantly, or exclusively, upon the diseased side.

Tumefaction of the auricular and submaxillary lymph-glands upon the diseased side has been determined, among others, by Walb, Haab (6 cases), Manz, Horner, Milligan, Luc, Niederhauser, Parinaud, Gayet, Mules, Stölting, Rhein (4 cases), Spangenberg, Hill Griffith, Burnett, Albrandt, Sattler, Braunschweig, Pregel, and others.

This disease of the glands is a notable instance of the analogy between clinical and experimental observations. I found it to occur constantly in our animals. If the major portion of the infective material is carried directly to the glands, while only a small part remains at the site of invasion, it may happen that the tuberculosis of the glands will give symptoms before the peripheral focus attracts notice.

Disease of the cervical glands may arise by retrograde propagation from the bronchial glands, but is *de facto* rarely so produced, as is shown by the fact that the cervical chain is rarely found to be implicated in cases of pulmonary tuberculosis in children. When both sets of glands are simultaneously involved, it is fair in most cases to assume a secondary focus of infection for the cervical group.

The infective material is conveyed to the tributary territory of these glands either in nutrition or in the air of respiration or by means of foreign bodies. For example, Steigenberger records the infection of a healthy, hereditarily untainted child through the milk of a phthisical wet-nurse; after two months the child developed cervical glands as large as hens' eggs, containing tubercle bacilli. In feeding experiments, likewise, Baumgarten, Wesener, and others have repeatedly observed tuberculous disease of the cervical glands. It is possible that the kissing of young people by tuberculous subjects may occasionally be responsible for the development of tuberculous adenitis.

Tuberculosis of the bronchial glands is much more rarely discovered during life, judging by autopsy findings; however, it constitutes by far the most common localization of the disease in childhood. In adults the lungs are the only organs which are attacked more than these glands. They are a common finding in the bodies of individuals dying of other diseases also. Loomis investigated the bronchial glands of 48 patients whose death was due to some other acute disease or to an accident, and was able by means of inoculation experiments (not above reproach, it is true) to demonstrate a tuberculosis previously undetected. Among 40 bodies, including 30 without tuberculous stigmata, Pizzini found that 42 per cent. showed evidence of a latent tuberculosis of the bronchial glands. I found the condition in four and Spengler in six children who died of diphtheria, sepsis, and peritonitis. According to Demme, the bronchial glands are diseased in 80 per cent. of the autopsies; very often this is the only demonstrable lesion. Steiner and Neureutter saw isolated disease of these glands in 36 out of 302 autopsies on tuberculous children, and Neumann saw it in 8 of 105 autopsies upon children supposed to be non-tuberculous. It occurs mostly after the first year of life, and from that time on counts its victims in very considerable numbers.

That it originates through infection by way of the respiratory passages is now no longer open to doubt (see page 180). Children are especially exposed to the danger of inhalation through their manner of crawling around on the floor, since the bacilli tend to seek the lower levels by force of gravity. I was enabled to establish this fact by means of the following experiment: After having distributed pulverized sputum, I exposed 5 rabbits at various elevations from the floor (10, 50, 100, 150 cm.), for the same period of time, and under conditions in all other respects exactly similar. The autopsies revealed irrefutable differences, inasmuch as the lowest animals showed by far the most profound set of changes, while those higher up showed a progressively diminishing degree of infection.

A complicating pulmonary tuberculosis is very generally the effect of a severe infection. I myself was able to determine the presence of an isolated tuberculosis of the bronchial glands in animals which I had exposed very sparingly to the inhalation of dried tubercle bacilli. The further extension of glandular tuberculosis, especially under certain conditions elsewhere specified,—for example, trauma or measles (see page 232),—may secondarily result in the involvement of neighboring areas of lung.

In adults the parenchyma of the lung is, as a rule, the primary seat of disease, the glands secondary. Nevertheless a number of cases of apparently primary tuberculosis of the bronchial glands have been described, even in old persons, as by Nowack in a man of sixty-one, and by Loomis in a woman of seventy-one.

The mesenteric glands are the seat of caseation very frequently, especially as before in the case of children. The cause of their infection lies primarily in the use of foods (milk) rich in bacteria, and in the swallowing of sputum by phthisical subjects. In the form of tabes mesaraica it constitutes a frequent cause of death in infancy.

Tuberculosis of the lymphatic glands of the body is of far less importance than that of the cervical, bronchial, or mesenteric systems. This, indeed, might be expected, on account of the diminished exposure to infection from without. For the same reason the cubital and axillary glands, which drain the hand, are more often affected than the popliteals. Thus, swelling of the axillary and infraclavicular glands followed upon an anatomical tubercle in a case of Gerber's, and, likewise, upon the infection of a sluggish ulcer of the finger of a sick-nurse reported by Holst. The cubital glands are not invariably involved in infections proceeding from the fingers, but tend to be affected especially in deep processes. The axillary glands drain the more superficial parts of the upper extremities (Lewin), and are generally implicated also in tuberculosis of the mammary glands (Volkmann).

Infection proceeding from the genital apparatus, especially from the penis or the testicles, is apt to cause tuberculosis of the inguinal and retroperitoneal glands: Schuchardt, Hamilton (tuberculosis of the testicles), Zweigbaum (vulva).

The femoral glands not rarely present very considerable swelling in arthropathies of the foot and knee, whereas in caseous processes of the hip-joint and of the patella, the original glands appear to be regularly affected (v. Bergmann). Lupoid foci do not in all cases produce tuberculous disease of the corresponding lymph-glands, owing to the resistance offered by the skin to the passage of the bacilli, yet in a fair number of cases they are affected by the disease.

Given a suitable set of conditions,—namely, the materies morbi and a susceptible individual,—infection both of the bronchial and of the cervical glands is especially apt to be induced by those of the infectious diseases which are associated with catarrhs of the respiratory tract. These include measles, croup, scarlet fever, diphtheria, and influenza. In most instances, however, they simply cause the lighting up of a previously latent tuberculosis of the glands, and general dissemination of the process. Other forms of mixed infection also modify the caseous process in the glands to a very marked extent, and may bring about extensive suppuration.

[Recently considerable attention has been paid to the relation of tuberculosis to Hodgkin's disease. In 1870 Murchison * first called attention to the association of periodical attacks of fever with Hodgkin's disease; subsequently Gowers,† Pel,‡ and Ebstein§ reported similar cases. Askanazy,|| Sternberg,** Musser,†† and Schur‡‡ have reported cases presenting the clinical picture of Hodgkin's disease, but which upon autopsy or upon examination of the discharges proved to be tuberculosis. Sternberg and Musser believe that the adenitis of Hodgkin's disease is of tuberculous origin, and

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* Trans. Patholog. Soc., London, 1870, p. 372.

† Reynold's System of Medicine, vol. v, London, 1879.

‡ Berlin. klin. Woch., Jan. 5, 1885, vol. xxii.

§ Berlin. klin. Woch., 1887, vol. xxiv.

|| Ziegler's Beiträge, 1888, vol. iii.

** Arch. f. Heilkunde, vol. xix, p. 21.

†† American Medicine, Jan. 4, 1902.

‡‡ Wiener klin. Woch., 1903, No. 5.

that this fact accounts for the irregular fever that so often accompanies the disease. Dr. Dorothy M. Reed* reported eight cases of Hodgkin's disease in which careful study of the glands failed to show the presence of tuberculosis, in spite of the fact that irregular fever had been present during life. She concludes that Hodgkin's disease is a clinical and pathological entity, and that when tuberculosis is present with it, it is an accidental association.

The negative results obtained by the editor from inoculation into guinea-pigs of glands removed from four cases of Hodgkin's disease lead him to agree with the conclusions of Dr. Reed.—Ed.]

INFECTION OF THE BONES AND JOINTS.

Infection of the bones and joints takes many different forms. All those affections which are variously characterized as caries of the bone, spina ventosa, tumor albus, fungus, strumous arthritis, scrofulous inflammation of the bones or joints, are all at bottom tuberculous. Their character was first surmised by Koch, later accurately determined by Damsch, by means of inoculation experiments, and firmly established—at least for spina ventosa—by the bacteriological researches of Schuchardt, Krause, Demme, Renken, and others. The demonstration of tubercle bacilli is often very difficult on account of the small number present in the tissues.

The tubercle bacillus settles in the small bones of the fingers and toes, where it gives rise to the characteristic picture of spina ventosa, in the metacarpus and metatarsus, in the orbital process of the superior maxilla, in the bones of the base of the skull, more rarely in the flat bones of the cranium, in the ribs, in the sternum, and with especial frequency in the bones of the vertebral column, in which it gives rise to the spinal loss of Pott's disease. Or it develops in the epiphyses of the long bones, especially in the spongiosa of the articular ends of the bones, while it has very slight tendency to attack the diaphyses (Kahn describes three such cases) or the flat bones. The joints become involved by extension of the osteal focus, or the synovia may become independently infected.

Shut off as they are from all means of communication with the exterior, the bones and joints are almost invariably secondarily infected. In the majority of the cases the lymphatic and vascular system conveys the infection, which is analogous to the metastases in the joints and in the articular ends of the bones which occur after gonorrhea or other infections.

* Johns Hopkins Hosp. Reports, 1902.

Many authors are inclined to hold the vascular system almost entirely responsible. This theory, however, is opposed by the fact that the invasion is not general. In acute general miliary tuberculosis the simultaneous localization of the bacilli in the bones and joints hardly ever gives rise to clinical symptoms, since the individual generally dies long before the local disease has become sufficiently developed.

When the lymphatic vessels act as the channels of infection, there is ordinarily some primary focus in the immediate vicinity of the osteal disease. Such a case is the one cited above from Ruge, in which a bony focus originated through infection by way of the pharyngeal tonsils. Caries of the processus mastoideus and of the petrous bone are mostly referable to tuberculous disease of the middle ear. In an infection proceeding by way of the vascular system it is of course immaterial where the primary focus is situated. A further consequence of this vascular invasion is the lighting up of numerous independent and widely separated foci throughout the body. On the other hand, a tuberculous focus in the bone or joint may also give rise by metastasis to a further infection of the osseous structures of the body, and, indeed, of the other organs.

Infection of the bony tissues has been experimentally imitated in animals by means of injecting tuberculous pus or sputum into the vascular channels, and at the same time producing trauma on various bones or joints. The sites of trauma developed into foci of disease. These researches, which have done much to further our knowledge of the means of infection, were carried on by Schüller, Krause, and Müller among others. In 67 autopsies which were done by König-Orth the affections of the bones or joints were found to be associated with older lesions in other parts of the body in 53 of the cases; that is, in 79 per cent. The lungs furnished the primary site in 37 cases, the glands in 21, and of these the bronchial glands were the most frequently affected. The genito-urinary apparatus was affected in nine of the cases; once alone.

There are frequently foci in the lungs, which must be regarded as the point of departure of the osseous infection. These foci may occur in the form either of well-advanced phthisical disease or of scarcely recognizable apical nodules.

It has long been customary to regard scrofula as the soil upon which the inflammatory affections of bone and joints are prone to arise. In the light of modern science, however, it is not the "diathesis," but the scrofulous glands and their bacilli, which furnish the etiological factor in these affections. Albrecht collected 325 cases of fungous inflammations of the joints, one-third of which were traceable to scrofula.

Rupprecht, Sprengel, and others have drawn attention to the scrofulous diseases of the skin and of the organs of special sense as points of departure for infections of the bones and joints. An etiological association between these two forms of the disease is indicated *à priori* by a number of facts. In the first place, the greatest number of affections of the bones and joints occurs at an age which coincides exactly with the period during which glandular disease predominates. Almost a third of the cases of bone and joint disease fall within the first ten years of life, and fully a half of the cases occur before the twentieth year (Billroth); the frequency of these affections diminishes progressively as life advances. What is frequently described as the "hereditary taint," which is by many considered a factor of some moment in the production of these forms of tuberculosis, may in reality be explained altogether differently, namely, as an infection by association. Even so, this hereditary transmission is by no means so common a factor as certain writers would have us believe. Dollinger found pulmonary tuberculosis to have been present in either parents or grandparents in only 97 out of 250 cases, and Unger found that only 11 of 54 cases had sprung from tuberculous parents.

The secondary character of the disease is not always distinctly evident. On the contrary, the disease is very prone to attack strong, apparently healthy, even flourishing, individuals, who present no evidence of any other focus of disease, and who are absolutely free from any hereditary taint.

As König says, this apparently unreconcilable discrepancy between the general condition and a local focus of disease—for example, the knee-joint—has led many physicians into the most deplorable errors of diagnosis. There are only exceptional conditions which may induce primary disease of these organs.

Middeldorpff relates a case of this kind, which has already been cited. A lad of sixteen, previously healthy and of sound antecedents, wounded his knee-joint with a hatchet, and then bound it up with his handkerchief. The wound at first healed kindly, but fourteen days later the knee swelled up, and a typical tuberculosis of the joint supervened.

A case described by I. Israel is in all probability also primary in nature. A boy suffered a fracture of the skull, and after three months tuberculous granulations appeared at the site of fracture: the further course of the case was marked by the occurrence of multiple foci in the bones of both feet and in the ribs. The site of invasion is not necessarily demonstrable. Just as I have shown that tubercle bacilli may find their way into the glands without leaving any external evidence of their invasion, so too they may in all probability enter the bony areas which lie directly underneath the skin, even though this occurs more rarely.

The variety of primary bony tuberculosis is not at all affected by the fact that the most careful autopsies occasionally fail to demonstrate any older foci. (In 67 autopsies on individuals who had died with tuberculosis of the bones and joints, partly as the result of operation, Orth found 14 in which there was no evidence of previous foci, such as might have been regarded as the sources of the infections.) The investigations of Pansini, Spengler, Kossel, and others have taught us that glands of almost normal appearance even, in healthy individuals, notably children, may harbor tuberculous foci. I myself found latent foci of this kind in four out of ten children who had died of diphtheria. Glands of this kind are liable to caseate and to perforate. They then give rise to the tuberculosis of the hilum of the lung typical of infancy, or the germs may be carried still farther by the circulation and lodge eventually in the bones or joints.

Now, we know that certain of the general infectious diseases are associated with swelling of the normal lymphatic glands, especially those of the neck and of the bronchi—of the respiratory tract. If such an acute tumefaction involves a bronchial gland already infiltrated and tuberculous, it is easy to imagine that the increased hydrostatic pressure will distend the parenchyma, and that the tense capsule will eventually yield to the strain and burst. The virus is then carried by various channels into the immediate environment, or even to distant tissues. Thus it is that measles, scarlet fever, and pertussis have of old been regarded as predisposing causes of tuberculous affections of the bones and joints. Measles seem to give rise to these affections far more often than scarlet fever (Sprengel). Thomas would ascribe the difference simply to the greater frequency of measles.

A similar explanation may be given for the not infrequent dissemination of tuberculosis following the puerperium; the screaming causing excessive variations of pressure upon the foci situated within the thorax and abdomen.

Trauma may also be considered a factor in the production of tuberculous foci in the bones and joints. We do not refer to such traumata as furnish a direct portal of invasion. Schüller showed long ago that non-penetrating traumata were not of themselves capable of inducing tuberculosis in an otherwise healthy individual. Even though he were "predisposed," some preëxisting caseous focus in the body is an essential condition. Similarly we must discard the notion that the bacilli circulate in the blood of a tuberculous individual, and simply lie in wait, as it were, for a trauma with the associated destruction of tissues to fasten themselves in the body. For we know, in the first place, that the bacilli are perfectly capable of developing in the injured tissues, in sound bone, if they can only gain a foothold; and, in the second place, such a condition is entirely contradicted by the experience of surgeons, since very considerable traumata in scrofulous or phthisical individuals (extensive destruction of the soft parts, which take months to heal, complicated fractures, etc.) do not become tuberculous even in amputations of tuberculous limbs; as long as the operation has been done in sound tissues, the wound does not degenerate.

Too great emphasis has often been placed on trauma. Sprengel very justly calls attention to the fact that those parts of the skeleton which are not exposed to traumatic influences, for example, the region of the wrist, are relatively infrequently the seat of tuberculous disease. The disease attacks the following regions, in the order of frequency: the vertebral column, the hip-joint, the small joints of the hand and foot, the knee, the long bones, the ankle-joint, the tarsus, and the elbow-, shoulder-, and wrist-joints. According to Jaffe, the vertebral column is affected in 26 per cent., the ankle in 21 per cent., the hip-joint in 13 per cent., the knee in 10 per cent., the bones of the hand in 9 per cent., the elbow in 4 per cent., etc. Could we not ascribe the predominance of tuberculous spondylitis and coxitis in the series rather to the proximity of frequently caseous lymphatic glands?

On the other hand, there is a tendency to overlook the question whether trauma might not, directly or by contrecoup, exert some effect upon a latent tuberculous gland. Thus, the same agency might simultaneously set the tubercle bacilli free from the injured gland, and give them egress into the general circulation, while it also tended to favor the local deposition of the bacilli, through injury to the blood- and lymph-vessels and through the formation of extravasations.

The deposition of the circulating bacilli in parts of the skeletal system which are already in a state of inflammation from some other cause is explicable upon the same general basis. These areas then become transformed into tuberculous foci. In the same manner multiple foci may arise, in case large numbers of the bacilli have found their way into the circulatory passages.

The suppurative processes, which essentially alter the picture, are in part referable to mixed infection. [Nathan Raw* and others believe that tuberculosis of bones and joints is caused by infection with the bovine bacillus.—Ed.]

INFECTION OF THE BRAIN AND OF THE MENINGES.

Tuberculosis of the central nervous system and of its fibrous envelopes presents itself in a variety of forms. There may be a widespread dissemination of tubercles, frequently associated with the production of a serous or of a fibrinopurulent exudate, a form which by preference affects the pia. Or, secondly, solitary tubercles may occur, more properly described by Virchow as conglomerate tubercles. Or, finally, the picture may be that of tuberculous abscess.

For the most part the nervous system is affected, not alone, but in the course of a general miliary tuberculosis. Edlefsen found that in 58 cases of meningeal tuberculosis in children, 46 (or 75 per cent.) presented the lesions of a general tuberculosis. In 122 cases of a general tuberculosis combined with tuberculous meningitis, caseous foci were discovered in 105 (or 86 per cent.).

When the nervous system has once become the seat of the disease, it gives rise to a set of symptoms which practically monopolize the clinical picture, so that the miliary tuberculosis of the other organs is often unrevealed until the autopsy. The infection of the meninges is, therefore, strictly hematogenous, and thus resembles that form of the disease which follows upon typhoid ulceration, upon pneumonia (Willich, Nauwerck), and upon puerperal fever. At times it is possible to find the tubercles directly in the blood-vessels (Chiari), a condition which, of course, establishes the hematogenous origin. The lumbar puncture of Quincke has made it possible to diagnose the tuberculous nature of the process *intra vitam* by staining the bacilli (Lichtheim, Fürbringer, Goldscheider, Fränkel, v. Ziemssen, Freyhan, Dennig, Schwarz, Slawyk, and Manicatide).

The primary focus to which the meningeal infection owes its origin has no definite location in the body, but any of the organs may be responsible. In many cases the lungs, in others the bones or joints, are the starting-point of the trouble. In exemplification of the latter, Bramwell describes the case of a girl who had caries of the wrist (not examined for tubercle bacilli), and who died later of a tuberculous meningitis; no other focus was present in the body. Tuberculous meningitis is not rarely the final stage of genital tuberculosis (Simmonds). It may follow upon tuberculosis of the nose (lupus) or of the larynx (v. Santvoord). Doutrelepont observed a young girl who died of a basilar meningitis, the only other focus being a lupus of the face. Frequently it follows upon a tuberculosis of the bronchial or mesenteric glands (Flesch, Grunert, and Panse), or upon a tuberculous pleurisy (Grunert). Abelin asserts that he has never seen a case of tuberculous meningitis or of acute general miliary tuberculosis in which the bronchial glands were not markedly implicated.

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* Brit. Med. Jour., Feb. 2, 1903.

The same determining factors as were described in connection with joint tuberculosis and with hematogenous infection in general are here also of prime importance. In particular, measles and pertussis are to be emphasized as those general diseases which most predispose to the occurrence of cerebral and meningeal tuberculosis (Wortmann and Marfan). The manner in which they are instrumental in releasing bacilli from some latent focus (*e. g.*, the bronchial glands) has been described above. Another important factor is trauma, and here also the caseous bronchial glands generally furnish the point of departure of the disease (Demme, v. Salis, Hilbert, Schilling). Nevertheless, one must be careful, as Henoch points out, not to interpret a purely accidental coincidence of lesions in such a light. Operative interference with tuberculous foci naturally has the same sequelæ. Eichenberg collected 14 cases of meningeal tuberculosis following upon operations on tuberculous processes in Hagenbach's hospital for children. It is especially common after resections of the hip (Berthod). Binaud saw a tuberculous meningitis follow upon the extirpation of a tuberculous pyosalpinx. Certain writers assert that it may be due to the employment of tuberculin (Rütimeyer and others). Of this there is no proof. At all events, among 420 patients treated with tuberculin, I have never seen anything of the kind, and this experience tallies with that of many other observers.

In addition to the hematogenous route, infection may take place from a neighboring focus, either by direct involvement or by growth along the lymphatics. In this connection we may mention the pial sheaths of Huguenin, which accompany the nerves and enter into relation with the extracranial lymphatics. Thus, for example, the sheath of the optic nerve (Robin) becomes continuous with the complex lymphatic system of the orbits, that of the acoustic nerve enters into relation with the perilymphatic spaces of the labyrinth, and the sheath of the olfactory nerve leads to the nasal mucosa. The sheaths of the entering vessels lead into the lymphatic network and glands of the neck.

Observations of this character are common. For example, Knaggs had a case in which an enucleation of the eye for tuberculosis of the iris was followed after six weeks by death from tuberculous meningitis. Machek reports three cases of iris tuberculosis, of which two died of meningeal tuberculosis, the operation of enucleation not having been permitted. There are also not a few cases on record in which the process in the meninges was secondary to a catarrh of the middle ear or to tuberculous caries of the ear-bones (Caspari, Leith).

Kossel describes a case in which tuberculosis of the middle ear, with caries of its walls, eventually caused thrombosis of the sinus. The wall of the sinus had become destroyed, and both the tubercle bacilli and the other bacteria concerned in the infection had invaded the thrombus, whence they were carried by the circulating blood to all parts of the body. In this case the brain itself was found intact. Roussel found an abscess of the brain with embolism of the second terminal branch of the arteria fossæ Sylvii in a man of twenty-three, who had an advanced phthisical process of the lung. Raab observed a basilar meningitis subsequent to the opening of a tuberculous mastoid. In the same way, Knapp had a patient with an old pulmonary tuberculosis, in whom the opening of a mastoid abscess was also followed by a basilar meningitis.

The passage of the bacilli from the cavum tympani to the pia mater may undoubtedly be mediated by the vessels in the carotid canal, and by the lymph-channels which surround these vessels (Körner, E. Meier, etc.). This is suggested especially by the meningitides following upon scarlatinal inflammations of the ear (Huguenin).

Inflammatory processes in the nose may likewise be the cause of meningitis. We know from the researches of Key, Retzius, and Schwalbe, that injections into the subdural space of the brain travel into the lymph-vessels of the nasal mucosa and also into the deep lymphatic channels and glands of the neck. Foa and Rattone produced meningitis in rabbits by inoculating pneumococci upon the mucous membrane of the nose. Demme states that he saw an acute tuberculous meningitis secondary to tuberculous ozena in a boy of eight months who had no hereditary taint.

A retropharyngeal abscess seems to have been the starting-point of a tuberculous meningitis in a case of Northrup's; caseous bronchial glands were, however, also present. Further, the cervical glands may originate an infection of the meninges. Either the bacilli make the transit along the lymph-channels, in which case their passage is marked by a bead-like series of glands; or caseous masses pass into the circulation, which explains the lighting up of general and of meningeal tuberculosis following upon the subsidence of the cervical glands, as we so often observe it.

An apparently primary tuberculous meningitis was observed by Warfvinge, and a tuberculous abscess of the brain by A. Fränkel. Alvarez found a solitary tubercle in a child of two and a half years, who showed no other symptoms of tuberculosis; Dürck had a similar experience in a man of forty.

It is possible that such apparently primary cases originate from undetected foci in other portions of the body. Thus latent foci in the glands, especially those of the bronchial group, are more frequent than microscopic inspection would tend to show (see page 226). Or, again, tubercle bacilli may find their way from the periphery to the brain along the lymphatics, the external portion of the invasion not being manifest by any lesion. The nasal mucosa is especially liable to permit an invasion of this kind. Since only isolated germs can be carried in this way, we must believe that the conglomerated tubercles are particularly referable to such types of invasion.

From all that has preceded, it follows naturally that infancy is in a very especial degree susceptible to tuberculosis of the brain. During this period of life the external coverings of the body are far more passable, the lymphatics are more viable to the germs, and generalization of tuberculous processes is in every way more free. Demme did a postmortem upon a girl of twenty-three days, born of a tuberculous mother, and found that the right lobe of the cerebellum contained an oval tumor of the size of a hazelnut, dirty yellow, soft, and of a tuberculous character, which he regarded as a fetal tubercle. It was impossible, however, to exclude a postmortem origin with mixed infection by other germs, a condition which often simulates a rapidly growing tuberculous focus.

Among 125 children dying of tuberculous meningitis, Edlefsen found only 8 (or 6.4 per cent.) under six months; and of these, only one under two months. Mixed infection seems often to give a distinct character to brain tuberculosis.

Since tuberculosis of the brain is especially frequent in the young, it follows that the source of infection is, as a rule, to be found in those individuals who most associate with the child, and thus heredity comes to be erroneously considered as the real factor of importance.

Tuberculosis of the spinal cord and its membranes is essentially similar to that of the brain, and etiologically is mostly derived therefrom.

INFECTION OF THE VESSELS AND OF THE HEART.

Our knowledge of tuberculosis of the vascular system is derived very largely from the researches of Ponfick, Weigert, Orth, and Mügge. The formation of tubercles may occur in the veins, especially in the pulmonary veins (Weigert, Hanau), or in the arteries (Weigert, Nasse, Herxheimer). Vascular infection presupposes the existence of a tuberculous focus in the immediate proximity of the vessel, from which bacilli force their way into its walls, and there give rise to tubercles. Ordinarily this is followed, especially in smaller vessels, by complete obliteration of the lumen. If this does not occur, the disorganization of the tuberculous growth sets free infected fragments, which then travel in the circulating blood. These fragments again gain a foothold in other parts of the vascular system, and give rise to further processes of the same sort. They are especially apt to lodge in the heart, or in the nearest capillary network. For the most part, the liberated fragments do not contain single bacilli, but rather conglomerates of bacilli, which become disseminated through the blood, invade entire capillary areas, and produce extensive miliary tuberculosis. [Simnitsky* has reported two cases of tuberculosis of the aorta, both occurring in the course of acute miliary tuberculosis. —Ed.]

In a case of Kamen's a caseous mediastinal gland became adherent to the posterior wall of the aorta, eroded it to the intima, and so produced a rupture of the vessel.

The tubercle bacilli rarely tend to settle on the endocardium or the valves of the heart, except in acute general miliary tuberculosis (Weigert).

Bacilli have been identified in cardiac thrombi by Weichselbaum, Birch-Hirschfeld, Klebs, Kotlar, and Chiari, and in endocardial investigations by Heller and Kundradt. Their etiological significance in the latter has been called into question by Grawitz and v. Recklinghausen.

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* Prager med. Woch., Feb. 12, 1903.

Tripier saw the typical tubercles in the valves of a consumptive with verrucous disease of the mitral orifice. Londe and Petit produced tuberculosis by inoculation of the deposits upon the mitral valve, and Courmont by those in the endocardium, both cases being consumptives. For the most part, these bacteriological findings may be ascribed to an invasion by the bacilli of preformed vegetations, which may be due to the irritant action of the circulating bacterial toxins (Hanot). Tuberculosis of the myocardium is as yet a rare observation. Mendez could find only twenty-two cases in the literature, to which he added two of his own In the left ventricle of a girl dead of miliary tuberculosis, Hirschsprung found a tuberculous growth, as large as a hazelnut. Claessen describes a growth of the size of a hen's egg, with tubercle bacilli and other partly caseous foci in the right auricle. Kaufmann records a tumor-like tuberculous infiltration of the wall of the right auricle, and Pollák a conglomerate tubercle almost the size of a hen's egg in the septum of the right auricle.

Most of the cases of cardiac tuberculosis occur in the young. Of 25, fourteen were under fifteen years of age, in a series tabulated by Pollák.

Infection of the heart is always to be regarded as secondary to some older focus in the body, even though the latter escapes detection.

CHAPTER V.

INFECTION.

The previous chapters have shown not only that experimental research gives positive evidence of the infectious character of tuberculosis, but also that a large number of clinical observations upon the various organs of the body establish an etiological connection between the invasion of the bacilli and the onset of the disease. The most important rôle in this connection is played by consumptives, because phthisis is most apt to lead to a general dispersion of the bacilli; and yet there has been a tendency in certain quarters to underrate the importance of contagion, or, better, of infection, in tuberculosis, and to assign it a secondary position. It is said that this mad terror of the danger of infection, this fear of bacilli, dates only from the discovery of the germ, whereas no man and no physician previously had a suspicion of the dangerous influence of consumptives. Stricker, for example, writes that the idea of contagion in this disease had never, in fact, been entertained by the vast majority of practising physicians; it was a notion which originated in the laboratory. Even to-day there is a long list of authorities—Aufrecht, Römpler, Haupt, v. Ziemssen, and especially Baumgarten—who absolutely deny the practical importance of infection in tuberculosis.

ANTIQUITY OF THE THEORY OF INFECTION.

The belief in the contagiousness of consumption is not a creation of modern science, but is as old as history. It is far from my purpose to enter at this place upon an historical excursion, nevertheless I may merely mention the following names in support of this statement:

Aristotle, Isokrates (*λέγοντες ὡσ πλεῖστοι τῶν θεραπενξάντων ταυτὴν τὴν νόσον αὐτοὶ προσδιεφθήρησαν*), Galen, Alexander Aphrodiseus, Avicenna (eleventh century), Hieronymus Frascatorius (1483–1553), I. B. Montani (1488–1551,—*per halitum concipiunt contagium, immo cum phthisici exspuunt*), Lazare Riviere of Montpellier (1589–1655), Jacobus a Partibus Foroliviensis (1547,—*morbus octavus contagiosus est phthisis sive ulcus pulmonis*), Lorenz Scholz of Rosenau (1598), Johann Schenk of Graffenberg (1665), Franz Vallesius of Covarruvias (1562), Daniel Sennert of Wittenberg (1572–1637,—*inter causas externas, quae proximae et solae pulmonem corrumpere et in eo ulcus excitare possunt, est primo "contagium"*), Zacutus (1570–1642,—*utrum phthisis sit morbus contagiosus? responde affirmative, "unanimi medicorum munitus voto"*), Olaf Borch in Kopenhagen (1715), Michael Ettmüller in Leipzig (1644–1683,—*contagiosa est exulceratio pulmonum phthisica . . . aut per halitum aut per sputum; hinc liberi cum parentibus, consortes et conjuges cohabitantes sibi invicem facile hoc malum communicant*), Bernhard Gladbach (1694), Richard Morton (1696), Salmuth in Braunschweig (1648), Sylvius (1614–1622), J. Manget of Genf (1652–1742,—*contagium etiam hunc morbum propagat; hic enim affectus, ut frequenti experientia observavi, lecti socios miasmate quodam inquinat*). J. B. Morgagni (1649–1748) and his teacher Valsalva both asserted that they objected to conducting autopsies upon consumptives on account of the danger of infection. Roncalli Parolino (1692–1763) of Brixen, Johannes Fortius (1677), Wilhelm Baillou (1538–1616), Johann Fernel (1497–1513), Anton Portal, Theophil Bonnet (1620–1689), Baron von Swieten (1700–1772), Josef Quarin of Wien (1733–1814), Daniel Metzger (1739–1805), Hugues Maret of Dijon (1726–1786), Chr. Vogel (1771), J. J. van den Bosch, Josef Raulin (1777–1823), Theophil Baumes (1777–1828), Peter Frank (1786), Benjamin Rush of Philadelphia (1745–1813), J. E. Wichmann (1799)—all of these, comprising physicians of every nation, and hundreds of others who lived before the beginning of the nineteenth century, championed the theory of the infectious character of consumption. They surely were not stricken by the modern terror of bacilli.

Whosoever wishes to find historical sanction for this attitude needs only to consult the works of the authors above quoted. Further, there is a wealth of similar material in the prize essay of Ullersperger, from which I have partly borrowed, in the excellent writings of Waldenburg, Häser, in those of Uffelmann and Leichtenstern, and in the fine history of tuberculosis by Predöhl.

These historical references are interesting reminders of the fact that at no time and in no century did the importance of contagion in tuberculosis escape the notice of the most celebrated physicians, and that it was clinical experience alone—which, indeed, furnished the only available criterion, of these times—that brought them to a recognition of this fact.

The lack of any exact knowledge upon the real nature of the infectious material naturally led our forefathers into the most extraordinary theorizings regarding the manner of infection. They pretended to localize the materies morbi in the sweat, in the urine, and especially in the exhalations of consumptives ("si phthiscus anhelat sanum, morbi propagationem minitantes"). Naturally, too, there were apparent inconsistencies and even contradictory assertions. During the era of the humoral pathologists especially, who attributed all diseases, including phthisis, to an abnormal constitution of the tissue juices, the theory of contagion was violently attacked, and the greatest significance was ascribed to hereditary influences. The vast majority of practitioners, nevertheless, held firm to their previous beliefs.

The doctrine of contagion is not an offspring of bacteriology, but is as old as medicine itself. Throughout the ages it has withstood the buffetings of hostile systems and of controversy. Nay, rather, it is to be considered as the parent of bacteriology; for it was the undeniable fact of the contagiousness of tuberculosis which furnished the stimulus to discover the cause, the bearer, of infection, until the tubercle bacillus supplied the explanation.

Even among the laity the belief in the contagiousness of tuberculosis is very widespread, and has maintained itself in spite of the fluctuations in scientific doctrine (Lichtheim).

Raulin (1777–1823) states that in Provence all the personal property of consumptives is removed from use after death, and that most urgent prophylactic measures are practised. In Portugal it was customary at that time to destroy the clothes and bedding of individuals dying of phthisis. In Italy even the walls of the room are considered infectious. Similarly in Chili, during the sixties, pulmonary phthisis was universally held to be infectious. In Poland (Lubelski) there has long been an idea that the clothing and bedding of consumptives carries the disease. In old Vienna (Pogacnik) there was an ordinance prescribing the destruction by fire of all clothes which had been worn by consumptives. The inhabitants of Lippe (Rühle) had so ingrained a fear of infection that no pauper would accept even the finest garments if they came from a consumptive.

In various countries official notification was demanded of the physicians, and its neglect was visited with the most severe penalties. In 1788 the city of Naples passed and enforced a law of this nature, upon the recommendation of the collegium medicum of the University, which declared consumption, as proved by all medical experience, to be infectious in the highest degree.

The question of the relative importance of contagion and of heredity was reawakened by the discoveries of Koch and of Villemin, and the urgent necessity of a revision of traditional notions became patent.

We must go into these relations somewhat in detail, inasmuch as the opposition of many physicians is to-day based upon the question.

JOINT INVESTIGATION.

An attempt was now made to settle the question by means of a general inquiry. In 1878 Holden questioned 500 physicians of the United States as to their views upon the inheritability of phthisis. In England, Humphry applied himself to his associates of the British Medical Association with the inquiry whether and how often they had observed cases of phthisis which seemed to argue for contagion, on the one hand, or for heredity and predisposition on the other. In Germany, v. Leyden inaugurated a similar joint investigation among the physicians. He did not limit himself, however, to the direct question as put to the American and English physicians, but requested definite data regarding each single case. Pribram, in Bohemia, followed his example, and Valin took up the inquiry in France, Rauchfuss in Russia. In Italy, Corradi resumed in 1884 an attempt at a collective inquiry into consumption, which he had proposed as early as 1868. Finally, there is to be mentioned the inquiry undertaken by the "Wiener medicinische Presse."

And what were the results of these vast collaborations which had been begun with such fond expectations and were invested with such bright glamour—of these "gigantic undertakings," as Humphry designated them? Let us see.

Of 500 American physicians, 250 replied, and of these, 126 affirmed the contagious nature of consumption. Of the 10,000 associates of the British Medical Association, 1028 returned answers, of which more than 100 were useless on account of vagueness of statement. Of the remainder 262 expressed themselves for the contagiousness of the disease. There were adduced 158 infections through marriage, involving persons without hereditary taint in 130 cases. The German joint investigation, which included 55 medical societies and 12 insane asylums in Germany, to which the physicians of Holland also contributed, at the suggestion of P. K. Pel, yielded all in all "about 200 replies" (actually only 167). This was according to the "preliminary," which turned out to be also the final summary. Of these, after elimination of the useless answers, 41 spoke for contagion as the cause and 24 apparently for heredity. I say "apparently" because the 24 cases which were adduced in support of inheritance by Oldendorff, the "referent" on hereditary transmission, admit so freely of an interpretation upon the basis of contagion that hardly a single one of them can be taken as irrefragable evidence of inheritance of the disease. Indeed, Oldendorff gives a detailed account of only 6 cases, the rest being shielded from a critical analysis. Since, however, he cites only these cases in actual evidence, one is entitled to demand something positive from them at least; but they, too, fail to exclude the possibility of infection.

Is it, for example, a sure indication of hereditary transmission if both parents die within one year of tuberculosis, and the son, twenty-eight years of age and a factory hand, shows indubitable signs of tuberculosis four years thereafter? And how is the possibility of infection excluded by the fact that four of the brothers and sisters of the father and seven of those of the mother, including one sister with her husband and fourteen children, all fell a prey to the disease, so that the entire family of peasants died out of existence? Does it not seem far more rational, in the absence of all further details, to assume that the essential cause of this endemic was contagion? If this is one of the best cases of a series collected so industriously and so carefully, what are we to conclude as to the proof afforded by those cases which are merely cited and not detailed?

Where are the "numerous" families in which all the children, through hereditary taint, became infected with tuberculosis and died, in spite of the fact that they had not lived together for years, and had never associated with one another, and had never been exposed to other sources of infection? Examples such as this should be at the disposal of "every experienced practitioner," if we are to believe the assertions of Haupt and of many other supporters of the doctrine of inheritance.

The cases which argued for contagion were analyzed by Meyerhoff. There were 41, including 23 cases of infection through marriage, 4 cases of infection of parents through the care of tuberculous children, 4 cases of infection of persons through the care of relatives, and 7 cases of infection of persons through the care of strangers.

The French statistics supply a somewhat richer yield. It is true that only 83 out of the 10,000 physicians embraced in the inquiry returned answers (Valin): of these, 57 embraced the theory of contagion, 18 opposed it, 11 left the matter in doubt.

The number of their observations amounted to 439, of which 213 spoke for infection, 226 against it. The 213 cases of probable infection were distributed as follows: Transmission as between married people, 107; between brothers and sisters, 38; between children and parents, 19; between distant relatives, 16; between strangers, friends, servants, 32; from man to dog, 1.

The joint inquiry instituted by the "Wiener medicinische Presse," at the suggestion of Schnitzler, led to no positive results; for it proves absolutely nothing that Schreiber observed 25 cases of "undoubted inheritance" when he gives no further evidence of this fact than that in 20 cases either father or mother, and in 5 cases both parents, were tuberçulous, the possibility of infection being simply ignored by him.

In Italy, the Societä italiana d'Igiene received 680 answers, of which 59 (8.7 per cent.) spoke for infection, 124 (18.2 per cent.) spoke against infection, 497 (73.1 per cent.) regarded heredity as the chief factor in the production of the disease.

These joint investigations afforded a very inadequate basis for the settlement of the question. Moreover, they were not planned in such a way as to elucidate the *relative value* both of *heredity* and of *contagion*—least of all those undertaken in America and England, which are in reality nothing more than an individual expression of opinion.

Far more effective were the investigations of v. Leyden in Germany, of Corradi, of Valin, since in them the chief emphasis was laid upon the individual case, an analysis of which was required. Any observations which seemed to argue for heredity or for infection were to be detailed at some length. By this means it would have been possible to gain a clearer understanding of the matter under debate if a sufficient number of cases were reported.

But the most important point, the comparative influence of heredity and of infection upon the genesis of consumption, the preponderance of one or the other of these factors, could not achieve elucidation in this fashion. This end could only be attained if a sufficiently large number of cases were available for analysis, and if, then, every one of them should be subjected to the most scrutinizing investigation regarding every possible contributing cause.

To accomplish this purpose, physicians would have to be notified that all cases coming under their observation, or all within a certain specified time, were to be analyzed upon that basis. Actually they were invited to contribute the most striking, decisive examples in their practices—the "star cases." It is, of course, evident that every case must necessarily be the product of either heredity or infection. A third possibility is not conceivable unless it be an autochthonous origin, a generatio equivoca of tubercle bacilli, which no physician of to-day would entertain.

The demands of a systematic investigation came closer to being satisfied by the inquiry inaugurated by Bartels and pushed by the society of Schleswig-Holstein. They requested physicians to submit all cases of tuberculosis presenting themselves within a certain term of years to an etiological examination.

To a certain extent it fell short of its purpose, for of the 336 physicians invited to participate only 261 acceded, and these sent in only a portion of their cases. All in all 3068 cards were returned for the years 1875–1877, as we learn from Bockendahl, who undertook the report after the death of Bartels. Of these, 825 were discarded on account of insufficient data. The available cases were distributed as follows: 1074 acquired (52.6 per cent.); 1059 inherited from parents or grandparents (47.4 per cent.). Unfortunately, these cases do not admit of critical analysis, the details not having been published. Such an analysis, however, is absolutely requisite for a proper estimation of their value, since we have already seen what curious craft can sail under the borrowed colors of "indubitable inheritance" (S. Schnitzler's joint investigation, Oldendorff, etc.).

Further, Bockendahl's report contains no details regarding the mode of extrauterine infection. All those cases are designated as "acquired" in which the family history was free from tuberculosis, while those in which it occurred pass as instances of "inherited tuberculosis." Bockendahl himself admits that a preëxistent family tuberculosis is no proof of inheritance; his system of grouping the cases is to be excused simply on account of deficiency of material. The possibility of infection through marriage is demonstrated by the fact that in 1666 marriages in which one party was tuberculous the other also became diseased in 134 cases. Such are the results of the great national inquiries, which were intended to summarize the experience of about 50,000 physicians.

INDIVIDUAL RESEARCHES.

We have still to consider the researches of individual workers. Leudet's investigations regarding the distribution of pulmonary tuberculosis in families embraced 312 cases of tuberculosis occurring in 143 families—of 1485 people in all. They are the results of a private practice extending over twenty years. In 55 families there was only 1 case of tuberculosis, while in 88 families there were from 2 to 11 cases. Among 74 couples only 1 was tuberculous in 61 cases, in 13 both, 7 of which had probably acquired the disease by this association. According to Leudet, there is hereditary transmission of phthisis in more than half the cases. Dissemination of the disease among families by contact is not the rule; dissemination through the marriage relation is certainly very rare. Infection seems to be indicated by the fact that in 33 families, of which 15 were hereditarily tainted, 73 children out of a total of 124 were successively stricken with tuberculosis within a period of from one to nine years. Leudet, however, fails to give accurate data in the cases classified as inherited regarding the element of time and regarding also cohabitation—in short, all those factors which are essential for a critical estimate of his conclusions.

The adherents of the theory of heredity have made frequent reference to a work of Riffel's upon the inheritability of consumption. Of this work, only so much: that the author "has convinced himself that the tubercle bacillus cannot be the cause of pulmonary consumption and of other tuberculous processes," but that consumption is absolutely an inherited disease. If parents and grandparents gave no evidence of tuberculosis, Riffel went back to the great-grandparents. And, finally, he recalls the fact that he had known consumptives whose names were not those which belonged to the family.

Then there is Bergeret d'Arbois, and especially Musgrave Claye, who gathered a large series of cases supposed to argue for contagion. In addition to these, there are innumerable scattered contributions, of which a treatise by Goldschmidt is especially commendable.

Thus, although clinical observations upon infection through association are adducible, their number is very small when compared with the 150,000 cases of death which are annually due to tuberculosis in Germany alone, and to the 1,000,000 contributed from Europe. This disproportion is in part explicable by the peculiar difficulties which attend a demonstration of infection in tuberculosis.

The source of the infection is generally difficult to locate. The consumptive, suffering only from a slight cough with expectoration, passes for a considerable time as a healthy individual.

Further, in cholera, diphtheria, and scarlet fever an infection reveals itself within a few days. In typhoid and in syphilis it is manifest in a comparatively short time. Cause and effect are thus closely associated in the other infectious diseases, and their connection forces itself upon the notice of even the most superficial observer. On the other hand, the spread of the tubercle bacillus is inordinately slow, and weeks pass before the primary tubercle has constituted itself. Months, a half year, a year, or more, elapse before the focus of disease has attained sufficient dimensions and produced symptoms striking enough to attract attention. During this interval of time it is probable that the victim has changed his abode, has become widely separated from the source of infection, or that the individual who communicated the disease to him has gone to the grave.

Perhaps, too, the reason lies in the fact that we have not sufficiently investigated and identified the exact conditions which govern the infection, and so cannot successfully appreciate each individual instance; and this is, in fact, undoubtedly the case. Thus, for a long time, even toward the end of the eighties, the air of expiration was held to be infectious. If this were the case, the doctrine of contagion would meet with innumerable contradictions; the exceptions would outnumber the regular cases. It is, therefore, incumbent upon us clearly to gauge the conditions underlying the transmission of the disease as they have been elucidated by the most recent researches. Even to-day there are widespread misconceptions upon the subject.

CONDITIONS GOVERNING INFECTION.

The recognition of the tubercle bacillus as the cause of tuberculosis lies at the basis of our modern attitude toward the subject.

We have previously shown (p. 81) that the belief in the ubiquity of the tubercle bacillus is unjustifiable. The air of expiration contains no bacilli, nor can they pass into the air from moist sputum. Bacilli are found, as a rule, only in places in which consumptives live, and only when they permit their expectoration to evaporate and dry. The micro-organisms are endowed with but a brief term of life, and succumb rapidly to a free exposure to light, especially to sunlight. Moreover, the danger from dissemination of sputum is considerably lessened by the fact that most of the contained germs are already dead.

The doctrine of ubiquity, in accordance with the facts just cited, is now largely discarded by current writings.

UBIQUITY OF CONSUMPTIVES.

There are, nevertheless, certain widespread misconceptions concerning the proportion of consumptives in the population, founded upon an erroneous deduction from statistics. Thus the number of consumptives in Germany is frequently estimated at 1,200,000, a number which lacks accurate confirmation, and which is in reality much too high. In many of the latest works* we find the following idea, often expressed in the identical terms: Since a seventh of mankind perish from tuberculosis, and since, in view of the frequent discovery of tuberculous foci in persons dead of other diseases, it is to be concluded that at least a third of our race is tuberculous, it follows that every one is at all times subject to the inhalation of the bacilli. But, since not all individuals become infected, it follows that infection by itself cannot play the chief rôle in the spread of the disease, but that, rather, a preformed constitutional condition determines whether or not the disease is to gain a foothold. This conclusion is mathematically fallacious. It is certainly true that about a seventh of all deaths are due to tuberculosis. This is proved by the general statistics of all countries in which accurate records are kept. It is also true that various pathologists have found tuberculous foci in a third of their autopsies. But whence come these figures? Entirely from the pathological institutes, in which the poorest of the poor are autopsied, a class of the population possessing a much higher percentage of consumptives than the average of the community.

It is wrong to argue from this autopsy material to general conditions. For example, in Prussia, in the quinquennium of 1880–1884, there died in the public hospitals in all 137,218. Of this number, those dying of tuberculosis, consumption, or hemoptysis amounted to 34,184. On the other hand, the number of deaths in the entire state amounted in all to 3,504,078, of which 431,210 were tuberculous. So that, whereas the population as a whole did not refer even an eighth of its mortality to tuberculosis, in the general hospitals a quarter was attributed to that disease.

In Austria, in the same fashion, 11 per cent. of the deaths in the population at large are ascribed to tuberculosis, and about 30 per cent. of those in the public institutions.

Further, it is erroneous to conclude from the fact that one-seventh or even one-third of mankind die with tuberculosis, that the same portion (one-seventh to one-third) of the living are so affected. Such a conclusion would be correct only in case those dying of tuberculosis had been victims of that disease from their first breath. This, however, is not the case; for it is well recognized that most tuberculous individuals are free from the disease during the greater part of their lives, and fall a prey to it only a few years before they succumb. If, therefore, we are to estimate at any given time the percentage of tuberculous individuals in a given part of the population, we must evidently count only those actually suffering from the disease, and not also those who are to become victims after the passage of years. It is on this account fallacious to assume that a fourth or a seventh of mankind is at any time tuberculous, and to reason hence that the probabilities of coming into association with the tuberculous are correspondingly great. A fair idea of the number of people with whom a tuberculous individual comes into contact may be, however, arrived at. (I include therein only such tuberculous individuals as really furnish a source of danger to their environment; the latent cases cannot be counted and are also of no importance in this particular regard.) The distribution of deaths due to tuberculosis is yearly about the same for each age of life. This figure permits us to form an estimate of the number of the living suffering with the disease,* if we multiply the number of those dying by the number of years of disease. Even taking into account all the cases in which the disease is prolonged over fifteen to twenty years, the average duration of the disease in adults cannot be placed higher than about three years, and in children even less. There is an enormous number of cases, as clinical observations very clearly show, which die of the disease within a few months, or in one or two years. It is not probable that this calculation will ever be shown to be very far out of the way, being based, as it is, on about 700 cases; nevertheless, accurate figures upon the duration of the disease in the various classes of the population is much to be hoped for.

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* Thus, Gärtner says that the inertia which has characterized the attitude of the governments in suppressing tuberculosis in the past partly depends upon the fact that every third or fourth man is infected.

We should, then, get an idea of the condition of things in Prussia corresponding in general to the accompanying table (page 251).

If we compare the number of those who have tuberculosis (columns 9 and 10) with the entire number of the corresponding social condition (columns 2 and 3), then we see (columns 11 and 12) the relative frequency of tuberculosis in the class in question (for example, 1 to 347 nontuberculous).

These figures show that the statement "every man lives to some extent in a community of the tuberculous" is without foundation.

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* Dettweiler gives the average duration of life of a consumptive as seven years. He informs me by letter that his material is all from the middle classes, and that he has made no exact computations. Goldschmidt reckons at least two years. As far as Leudet's data upon 488 consumptives allow of an average estimate, five years would cover the life-period of those in good circumstances, three and a half years those in hospitals. These figures are, however, too high.

AGES.	PRUSSIA. Summary of Years 1891-1892.									To Each Tuberculous Individual there are Nontuberculous:		To Every 1000 Nontuberculous Individuals, there are:	
	LIVING.		Dying of Tuberculosis.				Average Duration of Disease.	Absolute Number of Living Tuberculous.					
			Absolute.		To Each 10,000 Living.								
Years.	Men.	Women.	Men.	Women.	Men.	Women.		Men.	Women.	Men.	Women.	Men.	Women.
1	2	3	4	5	6	7	8	9	10	11	12	13	14
0–1	474,694.5	463,435.0	1,369.5	1,094.0	28.8	23.6	1	1,369.5	1,094.0	347	424	2.9	2.4
1–2	406,753.0	402,208.0	915.0	835.5	22.5	20.8	1	915.0	835.5	445	481	2.3	2.1
2–3	396,877.5	392,127.0	472.5	472.5	11.9	12.1	1	472.5	472.5	840	830	1.2	1.2
3–5	776,998.0	768,751.0	511.0	596.5	6.6	7.8	1	511.0	596.5	1521	1289	0.7	0.8
5–10	1,726,560.0	1,709,271.5	792.5	1,036.0	4.6	6.1	1	792.5	1,036.0	2179	1650	0.5	0.6
10–15	1,647,973.5	1,625,688.5	867.5	1,623.0	5.3	10.0	2	1,735.0	3,246.0	950	501	1.1	2.0
15–20	1,503,665.5	1,498,596.0	2,501.0	2,853.0	16.7	19.1	3	7,503.0	8,559.0	200	175	5.0	5.7
20–25	1,234,442.0	1,290,676.5	3,446.5	2,915.5	27.9	22.6	3	10,339.5	8,746.5	119	148	8.4	6.8
25–30	1,143,482.0	1,192,886.0	3,354.0	3,316.0	29.4	27.8	3	10,062.0	9,948.0	114	120	8.8	8.3
30–40	1,909,957.5	1,984,224.5	6,742.0	6,319.0	35.3	31.9	3	20,226.0	18,957.0	94	105	10.6	9.5
40–50	1,478,395.0	1,587,998.0	6,789.0	4,946.0	45.9	31.2	3	20,367.0	14,838.0	73	107	13.7	9.4
50 60	1,082,834.0	1,210,231.0	6,587.0	4,780.0	60.8	39.5	3	19,761.0	14,340.0	55	84	18.2	11.9
60–70	690,368.5	811,522.0	5,303.5	4,364.0	76.8	53.8	3	15,910.5	13,092.0	43	62	23.3	16.1
70–80	311,221.5	374,162.0	1,705.5	1,412.0	54.8	37.7	3	5,116.5	4,236.0	61	88	16.4	11.4
Over 80 unknown.	51,864.0 1,577.5	70,641.0 1,898.0	115.0 5.0	113.0 3.5	22.2 —	16.0 —	3 —	345.0 —	339.0 —	150 —	208 —	6.7 —	4.8 —
Total of the living, including all ages,	14,837.664.6	15,384,316.0	41,476.5	36,679.5	28.0	23.9	—	115,426.0	100,336.0	128.5	153.3	7.8	6.5

The chances of association with the tuberculous vary according to age. While only one case of tuberculosis occurred among 2179 boys ranging in age from five to ten years, at the age of thirty to forty years the proportion is 1 to 94, and from sixty to seventy years, 1 to 43.

Often this proportion is markedly diminished. Thus, according to Schlockow, there sickened:

	Average Yearly Membership.	Number of Tuberculous to 1000 Members.
In the Journeymen's Association of Upper Silesia, 1868–1875	36,161	2.0
In the Journeymen's Association of Lower Silesia, 1873–1875	13,824	4.1
Railroad employees of the Rhine 1873–1875	63,104	3.6

Wittenmeier found during nine years in the coal-area of Saarbrücken, with an average registration of 22,511 persons, that only 148 were treated for tuberculosis, so that in 10,000 miners there were only 65 tuberculous.

It is only when we compare these relative figures with the number of years which the individual has lived, when we consider the number and ages of those individuals with whom he has come into contact, that we get an average idea of the relative degree of exposure to infection.

This, however, does not say that the same relation expresses the danger of infection. The latter is made to appear far greater than it really is, for the figures given include the numerous cases of isolated tuberculosis of the bones, joints, skin, glands, gut, and meninges, and also the many consumptives who either have no sputum, often for considerable periods of time, or are careful to destroy it, and a large number of individuals, in the woods, who represent no source of danger to their environment.

And, after all is said, with how many persons does the individual come into daily contact, either through living or working with them? We must emphasize again, in this connection, that the chief source of infection is to be found in closed dwellings, and not in the open. (See pp. 83 and 84.)

The child of one to five years evidently comes into direct contact only with its parents, its relatives, and the domestics. If these are healthy, the child itself runs no risk of infection. Therefore, we generally encounter tuberculosis at this age only if the parents or the relatives who come into contact with the child are also subjects of the disease (pseudoheredity).

From the sixth to the fifteenth year, during which the child goes to school, the circle becomes widened so as to embrace the other children of the same class, numbering 30 to 40, and the teacher.

The personnel of the class does not change to any extent during the school-year; the daily session amounts to about five hours. According to the previous synoptic table, there is only one tuberculous individual in nearly 1000 living children of the age of five to fifteen years, and this one individual imperils only his immediate environment, *i. e.*, 6 to 8 children.

From the twentieth to the thirtieth years the extent of an individual's acquaintanceship will vary enormously according to the occupation and sex; but, as a rule, the number of persons with whom we come into close and continuous contact will hardly be found to exceed 8 or 10. It is, of course, true that 40 to 50 people work together in large factories or shops, and that among all of these probably at least one is tuberculous. According to one table, there is on the average one tuberculous individual among about 85 males and 109 females, ranging in age from twenty to sixty years; but this single case is a source of great danger only to his immediate neighbors. The danger diminishes centrifugally and in a ratio more than equivalent to the distance from the center of infection, inasmuch as the bacilli do not distribute themselves evenly throughout the atmosphere, but tend to gravitate. Thus I found tubercle bacilli in the immediate neighborhood of consumptives in sick-rooms, but none at any distance.

The exposure to infection is, therefore, less general than is ordinarily supposed; it is false to premise, as is done in almost every debate upon tuberculosis, that every person comes into frequent contact with the tuberculous, and would long since have been infected if the disease were really so transmissible. The conclusions drawn from this statement are, of course, also confounded.

THE DANGER OF INFECTION AS CONTROLLED BY THE INVALID.

The fact that there is one tuberculous individual to 85 to 109 adults does not mean that there is a corresponding danger of infection; for all consumptives who are careful with their sputum, either for sanitary or for esthetic reasons, are to be considered as almost innocuous. Those, too, who swallow their sputum, endanger themselves, but not their neighbors. Thus we meet with many men who have had most intimate associations with consumptives, and yet have not contracted the infection.

Infection is occasionally brought about when one individual directly coughs upon another, as Flügge has recently pointed out. I have previously dilated upon this possibility. But for the most part it is not the infectious sputum which clings to the mucous membranes of the larynx and the bronchi which is thus coughed out, but rather the mucus upon the palatal arches, which only rarely contains bacilli. As far back as 1889 I made certain experiments upon this subject, which have not hitherto been published. The results are as follows:

From a certain hospital I selected those individuals who were especially the victims of violent and explosive cough, by means of which small particles of mucous membrane are most likely to be torn out; I was also careful to pick out such as had an expectoration rich in bacilli. Each of them was instructed to hold the inner surface of a Petri dish before his mouth in coughing. For half an hour I superintended the experiment in person, for the rest of the day leaving it to the good-will of the patient. On the succeeding day the dish was washed out with about 4 cc. of sterilized water, and with the washings of each dish a guinea-pig was intraperitoneally inoculated.

All in all, I experimented with 18 patients. In two dishes, macroscopic inspection sufficed to disclose a number of fairly large dried particles of sputum. Inoculation from these dishes produced within six weeks an advanced degree of peritoneal tuberculosis in the guinea-pigs injected. The other 16 dishes were, as a rule, covered with a more or less dense coat of dried mucus. The inoculation produced tuberculosis of the peritoneum in two others of the guinea-pigs, while 14 animals were found at autopsy to be free from tuberculosis.

In another set of experiments I took 15 consumptives whose sputum was likewise full of bacilli, but was very loose in the throat, and let them cough upon Petri dishes in the same manner. The dishes were washed as before, with the usual precautions, and the washings intraperitoneally injected. The 15 guinea-pigs were killed after six to seven weeks, and it was found that they were all in a healthy condition.

As all the cases which were made use of in the above experiments were almost without exception very sick, and as the sputum was full of bacilli, and as only such cases were made use of in the first experiment as provided conditions most favorable for the dissemination of the germs—namely, violent cough—we may regard the result as confirmatory of that given above. Coughing only rarely serves to disseminate bacilli in sputum, and, if so, only in very small quantities. The danger of infection by this means is, therefore, of small moment, and may be disregarded in comparison to the enormous distribution of tubercle bacilli by means of dried sputum. But even the presence of dried sputum does not necessarily imply the infection of its entire environment except under certain definite conditions. We must pay greater regard than is usually given to the quantitative conditions.

Thus, it makes a great difference whether a consumptive expectorates only a few times a day or voids sputum to the amount of 400 to 500 cc., a hundred times as much; whether only isolated bacteria can be detected with the greatest difficulty or every field contains nests of bacilli; whether the case rapidly goes to pieces within a few weeks or voids sputum continuously for five to ten years; whether the case goes outside of his dwelling to pursue his calling or lives the entire day within his own room, with his family, to which latter group belong shoemakers, tailors, and domestics.

In proportion to the amount of time which the consumptive passes out of his home, by just so much is the danger to his direct family diminished. This may be a consideration of some moment, as there are cases, of which I have seen several, who are able to follow their work up to within a day or two of death.

So long as the consumptive is able to work, his occupation keeps him away from home for eight to ten hours daily, or, if he is a laborer, for fourteen to sixteen hours, which amounts to two-thirds of the day. The bulk of his sputum is, therefore, deposited away from his own home, the more so that many consumptives do not expectorate at all during the seven to eight hours of sleep. It follows from these facts that an ambulatory consumptive is a source of far greater danger for his co-workers than for his family. At times, though more rarely, the women of the family also follow an external pursuit. Berlin, for example, numbers about 270,000 self-supporting women, of whom 1400 are married.

It is easy to see that a phthisical father will be less likely to infect a family than a mother. This needs no forced theory upon the influence of the mother in heredity. Among the dense population of the lower classes, which are particularly subject to the danger of infection, diseased individuals are apt to seek medical care in the hospitals, where they remain many months, even until the end. In this way, again, the danger to the family is diminished.

But even when patients pass the entire day at home or in bed, they are often forced by the enormous quantities of sputum which they void to make use of some receptacle for it, and thus make at least a portion of it harmless.

DANGERS OF INFECTION AS MODIFIED BY THE ENVIRONMENT.

Not only the consumptive but also his environment play a rôle in limiting the danger of infection. The degree of danger to the household of a consumptive is measured by the amount of time which he passes at home. The husband is kept busy away from home for the entire day; the wife goes to the market or works in the kitchen during the morning; the children are at school for five to six hours, and romp for hours on the streets, especially if they belong to the lower classes; the grown-up relatives * have a calling which keeps them away from morning until night. Thus the "long months of living together" reduce themselves in many cases to a few hours.

Of great significance from the point of view of infection are the conditions in the dwelling and in the workshop, disregarding the denseness of population, which will be discussed under the "social aspect" of the question. Situation and sunlight are important factors. The more accessible to sunlight they are, the faster do the germs and the bacilli disappear; therefore, in a dwelling which is well ventilated and exposed to a southern light the consumptive will exercise a far less influence for ill than in a house lying in some dark and narrow alley, into which sunlight hardly ever penetrates.

Anders found that in Philadelphia the inhabitants of the broader streets contributed the smallest proportion of consumptives, and that the dwellers in the alleys had the greatest share.

Of equal importance are the degree of cleanliness, the methods of cleaning, and the time of cleaning.

The germ-content of the air varies with the time of day. Neumann estimated the number of germs to every 10 liters of air in the Moabitic Hospital, at different times of the day. Between 7.30 and 8 A. M., shortly after the rooms had been swept and the sick had got up and dressed, there were 80 to 140 germs. Toward 9 A. M. the number fell to 68. Between 10 A. M. and 12 M. the number ranged from 22 to 42. These three measurements were taken before, during, and after the medical rounds (see page 273). Between the noon meal and the afternoon coffee there were about 20 germs to 10 liters. Within two hours after the sick had gone to bed the air held only 4 to 13 germs to the 10 liters; in other words, it was as pure as in absolutely uninhabited rooms.

* In Germany, of every 100 persons between the ages of one and fifteen, three to four are bread-winners, and of every 100 between fifteen to twenty, 78 are in that class. So that a considerable number of the children of a family are busied outside of the home.

According to Stern, dust and the attached micro-organisms tend to seek the floor within twenty to thirty minutes of the time at which they were stirred up.

Richard tested the germ-content of the air in rooms during the making up of the beds, and found that 360 colonies developed out of 5 liters of air, whereas only 59 colonies developed out of 20 liters if the windows were kept open. He rightly argues that the danger of infection is about thirty times as great in the former case as in the latter, and he sees a similar danger in carpets and curtains. All these investigations hold for the tubercle bacillus as well as for other germs.

From all these researches we are perfectly entitled to conclude that vastly more bacteria are inhaled in one hour in a room which is undergoing cleaning than in the other twenty-three hours after it is completed.

It is, therefore, of great moment in determining the danger of infection whether the cleaning is done early, while the entire family is still in the house, or later, while the members are at school or in business, thus escaping the inspiration of the infected dust. *Mutatis mutandis*, the same conditions hold sway in the workroom. The bacterial content falls considerably during the time which succeeds the cleaning, and at night—the time of sleep and rest—it falls to practically nothing (Williams, Celli and Guarnieri). It is thus very illogical to attribute any especial degree of danger to sleeping with consumptives.

Much depends upon the mode of cleaning—whether one mops or sweeps, whether one keeps doors and windows open or closed. In the former case the air is, of course, much more rapidly purified of its dust.

Various as are the rules governing this domestic process, they remain fairly constant in any one family. From day to day, from month to month, the conditions which make either for health or for disease are added one to another, until, taken as a whole, they exercise really a determining influence. Decency and indecency, cleanliness and filthiness, pass as a heritage from generation to generation, and their effects often simulate an actual bodily inheritance.

Even if the bacilli are in the dust, they are not necessarily in the air, and if in the air, they are not always inhaled; and, finally, even if inhaled, they do not inevitably find their way to the deeper parts of the respiratory tract or to parts denuded of their epithelium, the only place where they are allowed to rest in peace and pursue their growth (see page 176).

We have already seen that unless the air be very dry (Infections of the Respiratory Tract, p. 181) the sputum is not sufficiently desiccated and divided to be capable of inhalation into the deeper parts of the respiratory tract. This is due to the fact that it contains considerable quantities of mucus and is also somewhat hygroscopic. In damp weather, in damp dwellings, in rooms heavy with moisture, either from the breaths of many dwellers or from cooking with steam, the sputum fails to be pulverized, and its inhalation is, consequently, made very difficult. Infection is, therefore, relatively rarer in such places, notwithstanding the fact that they may be extremely unhygenic in other ways.

Through neglect of this factor all the earlier inhalation experiments on animals with dry, pulverized sputum were unsuccessful (see p. 101).

There are, therefore, a large number of factors which influence the dissemination of the tuberculous virus and also its absorption by the body. Among these are the habits of the consumptive, the condition of his environment, the dwelling, the degree of cleanliness, climatic conditions, according to the combinations, favorable or unfavorable, of these various factors. Only by carefully appreciating such essential points is it possible to explain the apparently anomalous course and distribution of tuberculosis in families without at the same time having recourse to the hypothesis of predisposition.

I have made the attempt, in 800 cases of consumption which have come under my care, to determine the relative importance of heredity, infection, and predisposition. I shall illustrate, as occasion demands, from these records, in the succeeding pages.* I did not confine myself to the often imperfect anamnesis, but made physical examinations of all accessible relatives, fellow-workmen, etc., in some instances of as many as thirty persons. Further, I made a practice of questioning the associates, the municipal authorities, and all others who could help me, and thus I filled out the gaps in the case-records as far as possible.

The sources of infection may be subdivided into various groups, of which the most important are the following:

INFECTION THROUGH THE FAMILY.

Infection through the family naturally plays a very great rôle in the dissemination of tuberculosis, especially among younger individuals. It is in just such instances that one encounters the theory that hereditary conditions underlie the disease. I need not state, however, that it is hardly justifiable to regard a case as hereditarily acquired simply because tuberculosis is present in the parentage or in collateral relatives. Tuberculosis is so widespread that we must expect to find it in more than one individual in large families.

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* I hope to be able to publish the protocols of the cases more in detail at some future time.

A careful investigation of the actual conditions reveals many contradictions to the theory of heredity. I need only refer to the fact that children who are hereditarily tainted are apt to remain healthy when brought up in orphan or foundling asylums, unless their new environment subjects them to fresh dangers (see chapter on Heredity, page 316).

In a considerable number of my cases, including children born both of healthy and of unhealthy parents, the infection was derivable from the foster-parents or from step-parents, a fact which seems to yield new insight into the actual workings of heredity.

If one investigates a fairly large number of cases of apparently hereditary disease, it seems a strange thing that the parents often show the first signs of the disease years after the birth of the child. Indeed, the period of illness or the death of the parents often comes very close to that of the child. There are, of course, many exceptions, in which almost an entire generation may separate two cases in the same family; but if these exceptions, again, are analyzed, it will be found that brothers and sisters or near relatives, especially such as are intimately associated with the family, constitute connecting links between the diseases of the parents and of the children. The following case may serve to illustrate this fact:

Case 136. Entered 1892.* Augusta Vil, aged thirty-one years, married, wage-earner. Father died in 1887, aged sixty-four years, of old age and asthma(?). Father's parents died at a well-advanced age; mother's parents died early. Collateral relatives of father all healthy. Mother died of phthisis in 1877, aged forty-seven years. All collateral maternal relatives died of the same disease. One year after the death of the mother, a brother, aged sixteen years, died of tuberculosis; he had always lived at home. In 1879 a sister, aged twenty-five years, who had been married for three years, died of tuberculosis; she had been sick ever since leaving her parents' home. In 1883 a brother, aged eighteen years, died of phthisis; in 1887 a brother, aged thirty-five years, who was asserted to have suffered for fourteen years with cough and expectoration.

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* Statements concerning age, etc., are referable to the year 1892–3, the period of investigation.

The patient gave symptoms of the disease toward the end of 1889. The brothers and sisters associated together a great deal. The eldest sister, aged thirty-nine years, who had been away from home the longest, nursed the patient eight months previously during labor and puerperium. During the last few weeks she complained of cough and expectoration; physical examination revealed dulness and râles over the right apex, as low down as the second rib. It may further be mentioned that the brothers who died in 1883 and 1886, respectively, had lived with the patient for a considerable length of time.

Frequently it is not the parents who first fall sick but the children, who carry the disease into the family from the factory or wherever else they have acquired it; then it is only a matter of chance, depending on the intimacy of the family relationship and on the nursing, who first falls a prey to the infection. In the following case, for example, it was the brothers and sisters.

Case 99. Admitted 1892. John H., aged twenty-seven years, single, painter. Father died, at age of sixty-nine years, of carcinoma of the stomach; mother, aged seventy years, in good health; grandparents attained old age. One maternal aunt and one paternal uncle are healthy, likewise two brothers of the patient (aged thirty-one and thirty-two years), and also their children. In 1885 a married sister, who had lost her husband and three children through tuberculosis, fell sick of the disease. A brother, aged twenty-nine years, who had much to do with this tuberculous sister, was discharged from military service in 1886, married, and died in the same year of pulmonary hemorrhage. His wife also fell sick of tuberculosis. The patient under examination, who had often been with his tuberculous relatives for hours at a time, fell sick of an hemoptysis in 1888.

Again, the disease may pass directly to the parents, which is especially apt to be the case if they are much occupied with the nursing, or if the brothers and sisters absent themselves a good deal from the home.

Case 107. Admitted 1892. Ernestine R., aged sixty years, married, separated. Both parents of the patient died of old age, maternal grandmother in the puerperium, other grandparents at an old age. Patient had six children, five healthy, aged twenty-five to thirty-six years. Three of these children were examined and they and their families found healthy. One daughter of the patient had associated very freely with a tuberculous acquaintance (Ida F.), both in working hours and during her leisure time. Ida F. died, in the autumn of 1890, of tuberculosis; the daughter of the patient followed in April, 1891; and the patient herself, who had nursed her daughter and who previously had good health, fell sick of the disease in 1892, at the age of fifty-nine years. The other daughters of the patient, who had followed their respective vocations during the illness of their sister and who had come but little in contact with her, remain in good health.

The fact that only a certain proportion of the children, of the parents, and of the sisters and brothers are infected, while the rest escape, is very difficult of explanation upon the theory of inheritance. If, however, the family history be closely investigated, it will be found that the former were more closely tied down at home, either on account of youth or of vocation, etc., and that the latter—those who remained healthy—left home or were kept away throughout the day by their pursuits. Thus, in the following case the father and those of the brothers and sisters who were away from home remained in good health.

Case 8. Admitted 1892. Augusta C., single, aged twenty-four years. Mother died of pulmonary hemorrhage in 1885; maternal grandfather alive at the age of eighty-four years; maternal aunt alive and well; maternal grandmother died of cancer. Of the patient's brothers and sisters who live at home with the mother, only one, a boy, aged fifteen years, is in good health; one brother died at the age of sixteen years (1883), another at the age of fourteen years, both of consumption. The patient herself fell sick of tuberculosis in 1885, and traveled from home to live with a sister, aged twenty-five years, who has since then also succumbed to the infection.

On the other hand, a married sister, aged twenty-six years, who was away from home at the onset of the mother's illness, is healthy, as are also her children. Similarly, a brother, aged twenty-two years, at that time employed at his studies, is healthy; also a sister, aged sixteen years, who slept in another room; and the father, who slept in a separate room during the daytime and was kept busy at his work during the night.

The mother and children remained healthy in the following case:

Case 141. Entered 1892. Adolph V., aged twenty-three years, single. In 1884 his father died of hemoptysis and fatty heart. The latter was accustomed to spit on the floor and into his handkerchief. During the same year a sister, aged eighteen years, died, after an illness of a year's duration, and also a brother, aged twenty years, who had been taken sick a half year previously, both of tuberculosis.

The patient lived with this brother and sister. In 1889 he had his first hemoptysis. The elder sister, married since 1880 and living apart, is healthy. The mother, aged fifty-six years, who had until recently done washing from 6.30 A. M. until 9 P. M. away from home, was also in good condition.

If one accepts the standpoint of heredity, he is forced to assume that the disease will spare the elder children because they were born at a time when the disease of the mother or of the father was still fairly circumscribed, and that it will attack the younger ones, whose birth corresponds to the period of its development. As a fact, however, there is no such relation between the ages of the children and the ravages of the disease. As a rule, we find that it is those who have been least at home who escape.

CASE 43. Entered 1892. Marie H., aged twenty-one years, single, seamstress. Collateral relatives healthy, likewise four brothers, aged twenty-one to twenty-nine years, and five sisters aged three to eighteen years; grandparents unknown. Patient associated, more than any of the others, with a tuberculous father, nursed him until his death, and tended him at night. She had an hemoptysis in 1891, one year after the death of her father.

CASE 135. Entered 1892. Anna Br., aged twenty-seven years, single, seamstress. Mother, aged fifty-four years, healthy; maternal grandfather, aged seventy-two years, also healthy; maternal grandmother died of typhoid aged thirty-two years. Father, whose parents died at seventy-seven and seventy-five years respectively, fell sick in 1890, at the age of sixty-six years, of tuberculosis. In the same year occurred the death of a sister, aged twenty years, who had spit into cloths and who had been nursed by the patient. Patient tuberculous since 1891. The other children, aged twenty-one to thirty-two years—that is, both younger or older than the patient—are in good health and have healthy families. They remained away from home during the entire day.

CASE 129. Entered 1892. Martha Kl., aged twenty years, single, domestic. Mother died, in 1879, of tuberculosis, aged thirty-two years; the father in 1882, aged thirty-six years. Both expectorated on the ground and into cloths. Aunts and uncles healthy. One brother died, in 1888, of tuberculosis, aged twenty-four years; and the patient, who associated with him freely, fell sick of tuberculosis in 1888. Four children, aged twenty-two to thirty-six years, are healthy. One sister died in 1876, at the age of nine years, of typhoid.

Case 52. Entered 1892. Hedwig K., aged thirty-eight years, widow, seamstress. Parents reached old age; no tuberculosis in collateral relatives. Mother died in 1887, aged sixty-six years, of tuberculosis. Father then entered a hospital, and died in 1891, of tuberculosis, aged seventy-four years. The patient, who had lived with her father until 1887, had been with him during the entire day, and subsequently visited him in the hospital, fell sick of tuberculosis in 1890; while three unmarried children, aged thirty to forty-seven years—some of them, therefore, younger than the patient—are healthy, having had less intimate relations with the father.

Further, the fact that children near the same age fall sick of tuberculosis in succession is very naturally to be explained from the more intimate relationship existing between those of like years. It is entirely unnecessary to construct "a law of inheritance at corresponding ages." I have already pointed out that the parents are especially apt to infect the younger children. When these have grown up, they leave the parents' home, and then, of course, run the danger of infection from other sources. It may happen, however, that circumstances bring the parents and children together again late in life, and that these then infect each other, and so simulate a heredity of mature life.

Case 15. Entered 1892. Marie D., aged fifty years, domestic, single. No collateral tuberculosis. Father died, in 1844, of pneumonia; mother, in 1885, of tuberculosis, at the age of seventy-five years. Patient attended her mother until death. Previously healthy, she fell sick in 1888, at the age of forty-six years, of tuberculosis. On the other hand, two sisters, aged forty-seven and forty-eight years, respectively, who lived away from the mother, remain healthy.

Case 20. Entered 1892. Leopold W., aged forty-six years, married, coachman. Father died, in 1878, of consumption; also a sister in 1883, aged twenty-eight years. After the death of the latter, the mother, already tuberculous, moved from her house to that of the patient, where she died in 1884, at the age of sixty-one years, of tuberculosis. She had been used to spitting into her handkerchief in a way that was "perfectly disgusting." The patient, who was in the army from 1865 to 1868, has been sick since 1884. He was not often at home, and when there expectorated into the sink. Since 1890 he has been in the hospital. Wife of the patient, aged forty years, is healthy (examined), also five children, aged eight to eighteen years (examined). Two younger brothers, aged thirty-four and forty-three years, who have long been absent from home, are also well.

The same holds true of grandparents, as is shown by the following case:

Case 418. Entered 1892. Paul I., aged twenty-two years, single, tailor. Maternal grandmother lived alone, and died, in 1882, of tuberculosis. She was frequently visited during her seven years of sickness by the patient, by his fiancée, and by his two older brothers. The elder brother died, in 1888, of tuberculosis, after an illness of more than three years' duration. Paul I. and his older sister had scrofula (scars) as children, and both are now phthisical. The younger sister, however, who was only two to three years old at the death of the grandmother, and who rarely saw her, is healthy. The latter always slept with her parents, whereas the others lived together in one room. The parents, although both tainted through the mother, the paternal grandfather having also died of tuberculosis, are sixty-two and forty-seven years old, respectively, and are in good health (pseudoatavism).

In other cases tuberculosis is carried into the family through marriage, by sons-in-law, brothers-in-law, uncles, step-uncles, by friends, and especially by servants. It would be going too far, however, to illustrate every one of these possibilities with examples, though any number of these are at my disposal. The manner in which infection may invade the noblest houses is shown by a case which dates many years previous to the discovery of the tubercle bacillus, namely, to 1648. It is related by Salmuth, and concerns the Markgraf of Brandenburg. His words are:

"Tres Marchiones Brandenburgii adolescentes ex phthisi moriuntur, et brevi temporis intervallo unus nimirum post alterum; causa fuit relata in præceptorem phthisicum, quocum dies noctesque convixerant et eadem mensa perpetuo usi fuerant."

The statement that certain members of the family were away from home is not in itself sufficient to exclude the possibility of an infection through the family, to say nothing of an outsider, unless it can be established that no contact took place through visits.

INFECTION THROUGH MARRIAGE.

Transmission of tuberculosis by means of marriage has long been known. When a physician sees one of the partners of a marriage, and shortly thereafter the other, succumb to the same disease, the idea naturally suggests itself that there might be an etiological connection between the two cases. As early as the seventeenth century we find mention of the danger of infection through marriage in the writings of Ettmüller, Morton, and others. Jos. Quarin (1786) reports the case of a consumptive who infected a previously healthy and sound wife. After his death the woman married again and infected her second husband. After the death of the latter she married a third time, and finally died of consumption, the third husband following her. The contributions of Herman Weber, Villantin (infection of many women by one man), Drysdale, Castan, Baas, Holden, Bryhn, P. Drochon (several—two to four—healthy women infected by one husband), Burney-Yeo, Debove, Bennet, Wahl, de Lamarellée, Martin, Runeberg, and of many others who belong to the modern era, are well known. The number of cases of marriage infection, often of classical simplicity, runs up into the hundreds.

A general idea of the importance of marriage as a factor in infection may be gained from the following data: Of 159 couples, Brehmer found that in 19, or 12 per cent., both were tuberculous; Haupt found 30 cases in 260 couples, also 12 per cent. I personally investigated 594 couples, and found that in 135 cases, or 23 per cent., both partners were tuberculous, which amounts to double the percentage found by other investigators. These figures do not necessarily imply that there was always an etiological relationship between the cases. The discrepancy between my figures and those of Brehmer and Haupt is explained by the fact that their material consisted of well-to-do consumptives in health resorts, whereas mine was composed of hospitals cases, among whom infection is largely furthered by the unhygienic conditions of life.

As a fact, the percentage of cases in which both partners of a marriage are tuberculous is far larger than is indicated by the above figures. Closer investigation reveals the fact that of 459 couples in which only one of the partners was tuberculous, in 122 the other partner had already succumbed. Further, among 46 divorced patients, in 35 the tuberculous partner became ill after the separation. Therefore 157 couples are to be eliminated as not bearing upon the question of infection, an aspect of the case which seems to have escaped most of the writers. Further, it is to be remembered that in 40 of the cases one partner had been sick only one year, in 50 from one to two years, in 27 from two to three years; thus, the observation of these cases cannot be considered to be closed.

It is incorrect, on the other hand, to regard negative instances in the light of evidence against the contagious character of the disease. This error is the result of an exaggerated estimate of the intimacy of the marital relation. At the opening of this chapter it was pointed out that often the wife, but especially the husband, was apt to be kept away from home as much as two-thirds of the day; often man and wife met each other only at night, and even then they frequently occupy separate rooms, through disinclination, impotence, age, occupation, or other cause. Thus it is that the bond which holds the children, especially the younger ones, to the family hearth, is far stronger than that which unites the husband and wife. The position of the wife in the household is such that she is naturally far more exposed to receive infection from her tuberculous husband than to impart it to him.

As regards sexual intercourse, this may well be a source of danger to the genital apparatus, as has been previously shown, but practically never causes pulmonary infection. Moreover, the accepted notions concerning the infective power of a kiss is vastly exaggerated, since the saliva is generally free from bacilli, and even if it should contain bacilli they would be carried into the mouth and the digestive tract of the other person and not into the lungs.

With children the case is different. Their mucous membranes are far more susceptible to the bacteria, and it may be that kissing is not infrequently of moment in producing scrofulous cervical glands. But, so far as we are able to judge, this danger does not play any rôle among adults.

We see, therefore, that marital relations are not always so very intimate, and that a proper estimate of the actual danger of infection in every case can only be attained by weighing all the factors. In case the conditions which favor infection be present, then transmission of the disease takes place promptly. Of this we need cite only the following example:

Case 165. Entered 1892. William M., aged forty-two years, married, laborer. The family of the patient, including parents and three other children, is clear of any tuberculous taint. He married in 1871, and his wife died, in 1886, of phthisis. In 1888 he himself fell sick. In 1887 he married again, and in 1891 this second wife, also hereditarily untainted, showed signs of the disease.

INFECTION THROUGH THE DWELLING.

Just as infection may be transmitted among married couples or in families, so, too, it occurs among unrelated individuals who are accustomed to live together. In both sets of cases the essential element is the fact of living together. Infection by this means plays an especially important rôle among the lower classes, for with them overcrowding is very prevalent.

Thus, in one of the better, more recently constructed streets of Berlin the statistics regarding 805 laborers' dwellings, containing in all 3383 occupants, were as follows: There were 58 houses with single rooms; 657 dwellings which contained rooms for more than one individual, and of this number 301 were for more than four. In detail: 212, for 5 to 6 persons; 76, for 7 to 8 persons; 12, for 9 to 10 persons; 1, for 10 persons. In 42.75 per cent. of the dwellings there was an average of less than 20 cubic meters of air to each inhabitant; in 2½ per cent. there was not even one-half of the required minimum of 20 cubic meters.

It is not even necessary that the room should be simultaneously occupied by the consumptive and any one else. For weeks (six weeks) after the death of an uncleanly consumptive it is possible to find virulent tubercle bacilli upon the walls of the room, as I discovered in a certain poorly lighted dwelling which I examined relative to this point.

It is, of course, very difficult to obtain reliable information concerning the condition of health of the previous occupant. In a series of cases, however, I succeeded in accomplishing this.

The danger of infection in rooms rented unfurnished is far smaller than in those let furnished, on account of the cleaning up which preceeds each new occupancy of the unfurnished room; therefore students and unmarried officers especially are infinitely more exposed to such dangers than are others. Its actual extent can be gauged indirectly by regarding the floating population of Berlin, which consists of more than 133,000 souls,* from two points of view: First, as regards the percentage of the consumptive and of the uncleanly consumptive; secondly, the percentage of those who change their dwelling after a sojourn of one or two months.

Such cases of infection through the dwelling have been reported in considerable numbers, for example by Krücke and Engelmann.

Two consumptives died in a new, fairly healthy dwelling. Within the next twelve years there were 12 fatal cases of consumption among the actual occupants of the dwelling and those who had just recently left it (Engelmann).

I observed the following case:

Case 224. Entered 1892. Mrs. Juliana W., aged forty-two years, silver-polisher. Father died, aged forty-six years, in 1852, cause unknown; mother in 1866, aged forty-three years, of cholera; six brothers and sisters died young; one brother and one sister, aged about fifty years, are in good health. In 1889 the patient took a house previously occupied by a consumptive. She worked constantly in the house, and in the winter of 1890–91, she, too, fell sick of consumption. Her husband, aged forty-two years, who has been kept away from home by his vocation, is still in good health (examined), and a boy aged six years is also reported to be healthy.

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* Berlin Statistical Year Book for 1890.

INFECTION BY FELLOW-LABORERS.

The consumptive is far more a source of danger to his fellow-workmen than to his family. This is especially true of those callings which are followed within doors. From the mortality record of a number of Berlin mutual aid associations I extract the following figures:

Occupation.	Number of Deaths.	Number of Deaths Due to Tuberculosis.	Percentage.
Engravers	125	50	40.0
Waiters	259	117	45.0
Painters	53	25	47.2
Polishers	55	30	54.6
Book-binders	300	189	63.0
Cabinet makers and piano makers	1414	778	55.0
Upholsterers	2135	1314	61.5

On the other hand, among the masons and builders, who work more in the open air, of 543 deaths, 213 were due to tuberculosis (39.2 per cent.). Leupold found that in Pirmasens the mortality among shoemakers over twenty-one years was 12 per thousand of the living, whereas the remaining population of the same age had only 5 per thousand. The explanation is found in the fact that in the one factory 20 persons had only 5 cubic meters of air space apiece; in another 38 persons had 5.9 cubic meters each; 229 persons worked with less than 10 cubic meters of space apiece. The conditions were still worse among those working at home. How stealthily and surely the work of the tubercle bacillus proceeds may be seen from the following illustrations:

Case 295. Entered 1892. Bernard B., aged twenty-nine years, single, wood-carver. Mother died in 1875, aged forty-two years, after childbirth. Father died in 1885, aged fifty-two years, of gastric trouble. Neither the grandparents nor any of their children had shown signs of tuberculosis. A brother, aged twenty-five years, died of heart failure. Six brothers and sisters, aged thirty-five to eighty years, are sound. In the factory which employed the patient from 1887 to 1892, one of the employees died, in 1889, of consumption. Later on another also died, with whom the patient had had a great deal to do. In 1889 the patient had an hemoptysis. Since 1891 the master-workman, whose father died of old age at sixty-one years, and whose mother is in good health, has been afflicted with tuberculosis. In the autumn of 1892, Fritz St., who had been employed there for four years as an apprentice, became tuberculous. The establishment is large and well ventilated, but the workmen expectorate upon the floor, which is cleaned by sweeping.

Case 347. Entered 1892. Emil K., aged forty years, married, carpenter. Father, aged seventy-six years, mother, aged seventy-five years, are alive and well. Grandparents, aged sixty-six and sixty-nine years, dead, but not of thoracic disease. Two brothers and sisters, aged forty-seven and forty-nine years, respectively, healthy. One brother, aged twenty-six years, dead, cause unknown. Patient worked in a factory of Basch's. Basch began with a small factory in 1869, and from 1869 to 1878 was in partnership with Heymann.

1. Heymann died, in 1878, of tuberculosis.
2. Basch: father died at sixty years, not tuberculous; mother, aged seventy-five years, alive; brothers and sisters not tuberculous. Fell sick, in 1878, of tuberculosis, and died in 1889.
3. A workman named Gold died, in 1880, of tuberculosis.
4. A workman named Belke died, in 1885, of tuberculosis.
5. Emil K., the subject of this history, previously said to be scrofulous, had a seat near Belke. Fell sick, in 1886, aged thirty-four years, of consumption. Up to 1890, he worked off and on; he then became incapacitated, and died in 1892.
6. Hanof, in whose family there had previously been no tuberculosis, has been employed in the factory since 1886, and is at present (1892) tuberculous.
7. The eldest son of the master Basch, who continued the business after his father, is also tuberculous, according to the reports of the other workmen.

Emil K., having been warned by his physician and admonished by his wife, was in the habit of expectorating at home into a water basin. His wife, aged forty-six years, was healthy at time of record (1892); likewise two children, aged twelve and fifteen years.

In the factory in question, which until lately employed 13 men, there was no cuspidor, and the employees were accustomed to spit on the floor, which was swept up. As in many other instances, there was no explanation for the infection in the anamnesis. The conditions were only cleared up by an investigation of the factory and life of the laborers. It is, of course, true that bacilli are found especially and almost exclusively in places occupied by uncleanly consumptives. From this we cannot conclude, however, that an individual who is not conscious of having exposed himself to such associations has escaped the possibility of infection; for, in the first place, there is a large number of consumptives with infective sputum who are not recognizable as such without a careful examination by the physician, let alone the laity. Further, there may be an indirect sort of association, inasmuch as the consumptive has previously occupied the room, dwelling, establishment, etc. Finally, the dissemination of sputum may occur in still other ways, as by emptying cases of mull, in beating carpets and clothes, and in other ways, which all in all are of slight significance, but in individual cases may play a very important part.

On this account it is difficult to determine the source of infection in certain cases, since the disease declares itself only one-half to one year, or even more after infection, and the patient may then be living under entirely altered conditions. We must remember that it was very long before the contagiousness of syphilis received recognition, notwithstanding the fact that it is so apparent. In spite of all these difficulties, I was able to trace the source of infection in about half among 800 cases by carefully investigating all the correlated conditions and incidents; and when I failed it was in the case of individuals who had repeatedly changed their dwellings, or their situations, or whose former associates could not be discovered; there were, also, others who purposely falsified the anamnesis, because they feared that it might injure them professionally; finally, there were other cases in which, for various causes, the anamesis did not present itself with sufficient clearness.

INFECTION THROUGH OVERCROWDING.

More or less indirect evidence of the contagiousness of the disease is afforded by the high mortality rates which characterize groups of the population in which there is overcrowding. Thus the mortality from tuberculosis is as follows: In the penitentiaries of

Prussia, about 100 to 10,000 men; in the penitentiaries of Bavaria, about 150 to 10,000; in the asylums of Prussia, about 200 to 10,000; in the asylums of Bavaria, about 220 to 10,000. It was for a long time regarded as counterevidence that the rate of mortality in the penitentiaries was no higher than that in the prisons in which solitary confinement was enforced. Thus in the prison in Nürnberg, Haupt found a mortality of 80.4 per cent. from tuberculosis among the prisoners.

This position is fallacious, inasmuch as the number of the tuberculous has been compared not with the total number of the living but with the total mortality. The latter, however, is relatively small in the prisons on account of the lower age average of the inmates, and on this account the prevalence of tuberculosis seems exaggerated. Indeed, it is just in connection with this prison of Nürnberg that Döderlein, who was at that time physician there, was brought to combat the general conception of these prisons as breeding-places of consumption. He made a statistical table of all the forms of tuberculosis which had been encountered there in the previous twenty years, and found that of the 9692 inmates during that period, only 344, or 3.58 per cent., had fallen sick of pulmonary consumption.

Further, sufficient attention has not been paid to the fact that a considerable proportion of those who enter are already infected. In Nürnberg, 101 men were sick or suspected upon admission, and Döderlein's further observation, that prisoners are susceptible only during the first year of confinement, renders it probable that the majority of such cases were already infected when they entered. In the Moabite prison during the period 1875–1888, 56 prisoners died of tuberculosis: of these 20 were serving their first year, 26 their second, and 10 their third; therefore 46 (or 82 per cent.) died so shortly after admission that in all probability they were previously infected. Even among the other 10 (18 per cent.) the same possibility holds good, amounting even to a degree of probability.

Finally, isolation in prisons is by no means so absolute as is often assumed. The prisoner comes into daily contact with five to seven persons—physician, teacher, priest, overseer, superintendent, etc. Moreover, there is often a transfer for disciplinary reasons, which may also favor propagation of the disease.

The etiological importance of contagion in disseminating the disease is fully disclosed by the results which follow when the prisoners are permitted to do their work more in the open. Here the conditions which make for infection are reduced both in duration and in degree, and the mortality from tuberculosis falls correspondingly. Similar observations have been made in case of asylums and cloisters.

Grashey says that those of the insane who are able to get around and do their work are no more subject to disease than are the healthy; and von Ziemssen further affirms that those nuns who keep to the cloister are more apt to become tuberculous than those who have their work outside the walls. Are we to interpret these facts as instances of the "enormous rôle of predisposition," or do they not rather disclose the influence of contagion, which is most active in the closest confinement?

INFECTION THROUGH NURSING.

Those who devote themselves to the care of the tuberculous are especially prone to contract the disease.

It is true that the statistics of Brompton Hospital for a number of years past are cited as contrary evidence, inasmuch as they disclose an apparent immunity of the doctors and nurses. But the figures are, in the first place, too small; in the second place, the persons constituting the material were kept under observation for far too brief a period.

Under the direction of the government, an investigation was made into the Prussian Catholic hospital orders, which extended over about twenty-five years, and embraced 74,306 persons. It was found that tuberculosis was the cause of death in more than two-thirds of the cases, so that, as regards the expectation of life, a nurse of twenty-five years is on a par with a person of fifty-eight years outside of the cloister, and one of thirty-three years on a par with others of sixty-two years. By some this increased mortality has been ascribed to the conditions of life, the poor food, and the overwork.

A number of writers have been led to believe that the rate of mortality among the Evangelical nurses is not high. In this, however, they are mistaken, owing to the insufficiency of their statistics. A more extensive inquiry, which I instituted, has revealed the fact that the Evangelical sisters also pay a high tribute to the disease, although the mortality, thanks to the more healthy conditions of life prevalent among them, is not as high as it is in the Catholic sisterhood. Of 195 deaths, 82, or 42 per cent. were due to consumption. There is also another factor which tends to reduce the rate among the Evangelical as compared with the Catholic sisters. The vows of the latter bind them for their entire lives, whereas about one-half of the former (1963 out of 4000 in one year) leave on account of sickness or other conditions. Thus it is especially those who have recently contracted tuberculosis that disappear from the statistics. Accurate data, are therefore, excluded.*

The yearly mortality in the Catholic orders from tuberculosis formerly amounted to 150 to 160; now, with improved prophylaxis, it has fallen to 60 to 70 for each 10,000 living nurses. This cannot be explained except as a diminution in the amount of exposure to infection, since the conditions have remained unaltered.

INFECTION OF PHYSICIANS.

It has been said that physicians would necessarily present a high mortality from tuberculosis if the danger of infection were really so great as represented. The danger to physicians, however, is in reality, not nearly so great as that to the nursing staff. They have only brief communications with the patients, and that, too, at a time when the atmosphere of the wards is fairly free from germs (see p. 256). On the other hand, the experience of many observers (Fräntzel, Gerhardt, Grasnick) yield examples of such cases, and not a few of the physicians who practise in the sanitaria have gone through tuberculous attacks.

A number of writers (Brehmer, Haupt, Michaelis, etc.) have urged that the mortality among the inhabitants of the health resorts has not been increased, notwithstanding the constant circulation of consumptive visitors. If we consider the difficulties which beset an impartial and efficient estimate of this kind in a "health resort," the natives of which believe that their most precious interests are thereby imperiled, we shall accept such negative reports with the greatest reserve. The bona fides of the physician does not enter into the question.

The statistics are open to objection on still other grounds. If they go back a century, as Brehmer's do, and depend upon the church records of disease, the distribution of sickness is almost entirely within the discretion of the compiler. For example, there are a number of terms, such as pulmonary suppuration, pus thorax, internal ulcer of the breast, abscess of the lung, neurotic pus chest, etc., which might be excluded by one individual, although another would suspect them. Errors of this kind might be sufficient to obscure the truth when the data are compared with the very meager living population in such places.

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* A computation based upon the condition of the living could not be successfully made. Valuable communications have come to me from Königsberg, Danzig, Bethany in Berlin, Lazarus Hospital in Berlin, Posen, Bethany in Breslau, Frankenstein, Flensberg, Cassel, Frankfurt a. M., etc.

There are also flagrant violations of the principles of statistics in some of the reports. Römpler, for example, attempts to show that, though the population of Görbersdorf had doubled in the previous decade, the mortality from phthisis had fallen by more than half within the previous fifteen years. From 1790 to 1889, in a total mortality of 1002 there were 72 adults, the tuberculous being in the proportion of 1 to 14. Children up to the age of ten years are excluded from this calculation, inasmuch as the diagnosis was uncertain and "infant mortality due to tuberculosis is well known to be free from extraneous influences." In the last fifteen years, 1875–1889, Römpler includes 135 children among the 207 deaths; of these, 11 were due to consumption, and this brings him to the conclusion that in every 19 deaths there is 1 from consumption.

Haupt has also made up a set of statistics, with the avowed attempt to overthrow the doctrine of contagion. These statistics reveal, although the author himself fails to appreciate the fact, that of the 703 persons (housewives, servant girls, nurses, etc.) who had been connected with the care of the sick in Soden during the forty years before, 71 had died, 18 of tuberculosis. In Soden itself 48 had died within three years, 4 of tuberculosis. According to my own way of thinking, these figures, meager though they are, would seem to show that in the second series—*i. e.*, Soden at large—4 in 48 deaths, or 8.3 per cent., were due to tuberculosis; while in the first series—*i. e.*, those especially connected with the consumptives—the ratio was 18 to 71, or 25.3 per cent.; in other words, tuberculosis was the cause of three times as many deaths.

Then there is a set of observations which are absolutely at variance with those just related. Thus, Gericke relates that he was informed in Soden that the majority of the inhabitants died of consumption. Bennet found that there was an enormous increase in the mortality from tuberculosis in Mentone, although he attempts to explain it as due to other causes. Rochelt refers to the tuberculous infections among the washerwomen and chambermaids in Meran. According to Czernicki, physician in Cannes, tuberculosis was a very rare disease among the native persons up to 1860; from that time, which marks the beginning of the winter invasion by consumptives, the disease has become frequent. C. Spengler details his own experiences of twenty-five years and those of his father, relative to Davos. The place was originally free from tuberculosis, and the disease was gradually imported, as is shown by many examples. In San Remo, also, an increase in tuberculosis is asserted to have taken place among the inhabitants; this, too, is denied.

According to our previous argument, it is not the natives, the house owners and renters, who are especially subject to danger. They have very little to do with the invalids in their rooms—at most during cleaning. Moreover, the rooms in the villa-like houses of the "curorte" are mostly larger and brighter than those in the narrow streets of the city. The vitality of the bacteria is accordingly less in the former, so that, even though the rooms are again occupied by the owners after the departure of the consumptives, the danger of the infection is notably less, *certeris paribus,* than in the city. The servant girls are those most in peril, for they make up the beds and attend to the rooms. They do not, as a rule, come from the native population, but are imported for the season only. If sick, they are sent home. Thus, in one of our largest "curorte" I found that of about 500 girls, who came for the year, only about 120, or 5 per cent., were native-born, and only about 12 per cent. returned the succeeding year. How then, can we construct satisfactory statistics from such material? I recall my experience in Görbersdorf, where I repeatedly discovered a commencing apex-catarrh in girls who came from Waldenburg and Breslau.

Finally, I might cite the reports of various travelers that certain peoples—as, for instance, the natives of Tahiti, New Zealand, and the American Indians—first learned to know tuberculosis from the Europeans, and came to regard the coughing white man with terror. There is a recent confirmation of this mode of importation in the following observation of Alison's. In small places where for years there had been no phthisis, a single case of consumption imported from without would start a train of tuberculous infections. Those in the same house, or the neighboring houses, and especially persons who had come into close and continual contact, were the first to be affected.

INFLUENCE OF AGE AND SEX.

It follows that age and sex exercise a very important influence in determining the degree of danger to which each individual is exposed, and, that, consequently, the frequency of tuberculosis varies enormously with differences in these two conditions.

STATISTICAL ERRORS.

There is a general tendency to transfer to the living population statistics gained by a comparison of the mortality records. Such an extension is permissible only when the number of the dead is brought into actual numerical comparison with that of the living. Inasmuch as this error is especially widespread in the literature of tuberculosis, and frequently furnishes a fund of false and injurious arguments, it may be well to devote a few more words to it.

Thus, in attempting to estimate the distribution of tuberculosis according to age, a comparison is often made between (1) the number of those dying of tuberculosis within certain age limits and (2) the total number of those dying of tuberculosis, including all ages.

The data for Prussia in 1896 are as follows. In every 100 deaths of each sex there are:

Sex.	Under 1 Year.	1 to 2 Years.	2 to 3 Years.	3 to 5 Years.	5 to 10 Years.	10 to 15 Years.	15 to 20 Years.	20 to 25 Years.	25 to 30 Years.	30 to 40 Years.	40 to 50 Years.	50 to 60 Years.	60 to 70 Years.	70 to 80 Years.	Over 80 Years.
Male	3.29	2.00	1.02	1.18	1.87	2.10	6.59	9.52	8.23	16.90	16.79	15.51	11.47	3.32	0.21
Female	3.10	2.20	1.29	1.46	2.93	4.41	8.43	9.56	9.68	17.76	13.15	11.96	10.31	3.45	0.31

To reason from such a set of figures to the distribution of tuberculosis according to the same ages in the living would be justifiable only in case there were an even distribution of the population thoughout the various age-strata of life. The basis of the results would be the same. Such, however, is far from being the case. Thus in Prussia, in 1896, in the various ages, there is the following distribution of the population:

Age.	Number of Living.	Percentage of Population.
0– 5 years	4,277,994	13.42
5–10 "	3,684,679	11.55
10–15 "	3,315,814	10.39
15–20 "	3,164,252	9.92
20–25 "	2,745,817	8.61
25–30 "	2,450,437	7.68
30–40 "	4,185,621	13.13
40–50 "	3,189.385	10.00
50–60 "	2,452,668	7.69
60–70 "	1,542.277	4.84
70–80 "	749,377	2.35
Over 80 "	134.148	0.42
Unknown	1,711	0.00
Total	31,894,180	100.00

In other countries the distribution is approximately the same. According to official data, 7693 persons between sixty and seventy years of age died of tuberculosis; between the ages of five and fifteen years, 3893—*i. e.*, about one-half. Calculated in percentages of the total number of deaths from tuberculosis (absolute, 70,373), there are 10.9 per cent. between sixty and seventy years and 5.5 per cent. between five and fifteen years, again one-half. From these figures the conclusion is drawn that tuberculosis between sixty and seventy years has a significance just double that between five and fifteen years.

This conclusion is fallacious. There are about one and one-half million persons between the ages of sixty and seventy years, and about seven millions between the ages of five and fifteen years; that is, there are in the latter category five times as many living beings as in the former. Thus, while the 3893 deaths from tuberculosis are distributed among seven millions, the 7693 are derived from only one and one-half millions. For the latter class, therefore, ranging in age from sixty to seventy years, the death rate from tuberculosis is not only twice as great as that in the former, but actually ten times as great.

There is still another error which frequently recurs in the statistics of tuberculosis. In order to obtain a measure of the significance of tuberculosis, of its frequency, of its local distribution, of its ethnological distribution, and of its distribution in terms of years, it is customary to compare the number of deaths from tuberculosis with the total mortality. The average figures for Prussia in the decade 1881–1890 are as follows:

PERCENTAGE OF DEATHS FROM TUBERCULOSIS ACCORDING TO AGE AND SEX.

SEX.	UNDER 1 YEAR.	1 TO 2 YEARS.	2 TO 3 YEARS.	3 TO 5 YEARS.	5 TO 10 YEARS.	10 TO 15 YEARS.	15 TO 20 YEARS.	20 TO 25 YEARS.	25 TO 30 YEARS.	30 TO 40 YEARS.	40 TO 50 YEARS.	50 TO 60 YEARS.	60 TO 70 YEARS.	70 TO 80 YEARS.	OVER 80 YEARS.	TOTAL.
Male	1.0	3.0	3.5	3.3	5.1	12.5	35.8	45.2	46.6	41.0	33.6	28.4	19.3	6.3	1.2	12.7
Female	1.0	3.1	3.9	3.8	6.6	20.3	43.3	42.6	42.8	38.3	32.4	25.1	15.4	4.4	0.9	11.9

This ratio between the mortality from tuberculosis and the total mortality gives no accurate picture of the significance of tuberculosis, for it is affected by conditions which have not the slightest connection with tuberculosis.*

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* The same holds true of every other disease.

Thus, whenever the total mortality changes on account of a variation in the distribution of some other disease—*e. g.*, diphtheria—the percentage of deaths from tuberculosis becomes altered in inverse terms.

Illustration.—In a city of 10,000 inhabitants the total mortality in a certain year was 250; the mortality from tuberculosis, 25, giving a mortality from tuberculosis of 10 per cent. In the succeeding year, cholera or typhoid breaks out in the town and adds 100 deaths to the list, raising the total mortality to 350. Tuberculosis again claims 25 victims. Thus, in this year the mortality from tuberculosis would amount to only 7.1 per cent. Apparently the disease would have shrunk considerably in extent, although actually its distribution would be the same.

Another illustration of a different tenor: In Munich, typhoid, which once played so large a rôle there, has been almost eradicated, and the total mortality in proportion to the population has fallen. Now, notwithstanding the fact that tuberculosis has remained stationary or been somewhat diminished, its percentage relation to the entire mortality has risen from about 12 per cent. to 15 to 16 per cent. As a fact, we meet with the belief (Müller) that typhoid in former days would interrupt a well-advanced tuberculosis, and that at present tuberculosis gains the number of victims which would have fallen a prey to the intercurrent disease.

As regards age and distribution, the following example: In Prussia, between the ages of ten and fifteen years there died, in 1892, in all, 10,957; of tuberculosis, 2335, or 21.3 per cent.; in 1896, in all, 9716; of tuberculosis, 2229, or 22.9 per cent.

Apparently tuberculosis is on the increase. Actually it has lost ground, not only in absolute numbers, but also in proportion to the number of living; from 7.2 per thousand it has fallen to 6.7 per thousand. The fallacy is deducible from the fact that the mortality from diphtheria amounted to 1497 in 1892, and fell to 794 in 1896, thus lowering very considerably the total mortality.

Lack of a better method occasionally excuses the use of this one, and I myself have been compelled occasionally to employ it in this work. Nevertheless, one should always be aware of its shortcomings and hestitate to draw far-reaching conclusions from it.

SIGNIFICANCE OF TUBERCULOSIS ACCORDING TO AGE AND SEX.

A correct impression regarding the significance of the mortality from tuberculosis can be gained only by comparing the rates of mortality from the disease among various groups of population, either at different periods of life, or within two separate terms of years, upon an equal basis of the living population (say 10,000).

Lehmann in Copenhagen and Würzburg in Berlin have the credit of being the first to demonstrate the value of this method of reckoning.

The table on page 280 exhibits the mortality from tuberculosis according to age and sex, and, at the same time, the number of wage-earners within the same groups; the indisputable importance of the latter will become manifest later on. The tables are based upon an average of the figures upon tuberculosis for the last sixteen years in Prussia, and upon the statistics regarding wage-earners in the German census.

During the first year of life, in which the association between mother and child is the closest, and the degree of infection springs from the mother, we find a mortality which corresponds to that of the years of pregnancy. It falls a little below, because tuberculous women are less likely to have children than are the nontuberculous. Nor must we forget that the tuberculosis of infancy has an extremely rapid course, rarely more than a few months.

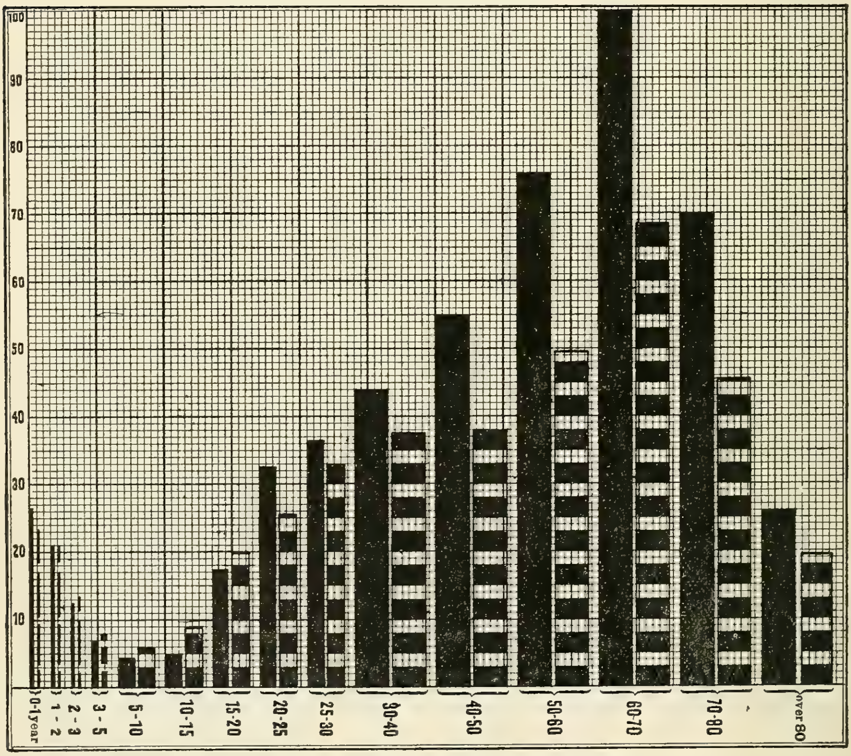
As early as the second year of life, with the first steps, the child becomes less closely attached to the mother. The mortality reaches 20 to 10,000, and is alike in both sexes. These figures vary somewhat with the degree of care bestowed on children, with climate, and other conditions.

The mortality in the third year is even lower. But even at this age a difference between the two sexes makes it evident, since the girls come into more intimate contact with the mother than the boys. The mortality among the former, 7.95 per cent., is therefore, greater than among the latter. This difference constantly increases. The boy, at the age of from five to ten years and over, seeks his play on the street with his comrades; the girl is held, both by custom and by inclination, to the house. Consequently, the mortality from tuberculosis is almost half again as great among girls from the ages of five to ten years; from the tenth to the fifteenth year, during which time the boy enjoys an even greater degree of freedom, the female mortality is almost twice as great.

From the fifteenth to the twentieth year the mortality rises rapidly; at seventeen years, for example, it reaches 19 per ten thousand. Moreover, the figures for both sexes tend to approximate, owing to the fact that a new element now influences the result. This new element is the boys' earning ability. Among boys, there are 897

	Mortality from Tuberculosis to each 10,000 of Living Population:				To each 10,000 there are: Wage-earners and House-workers.	
Age.	Male.	Female.	Male.	Female.	Male.	Female.
Under 1 year	26.40	22.94	8.85	10.44		
1 to 2 years	20.89	20.85				
2 to 3 "	12.45	13.54				
3 to 5 "	6.87	7.95				
5 to 10 "	4.52	6. 0			402	256
10 to 15 "	4.89	8.93				
15 to 20 "	17.63	19.80			8966	6672
20 to 25 "	32.32	25.34	34.68	29.14		
25 to 30 "	36.62	32.82			9685	4659
30 to 40 "	43.54	37.54			9781	2173
40 to 50 "	54.70	38.10			9715	2403
50 to 60 "	75.88	49.52			9378	2776
60 to 70 "	99.65	68.33			7989	2436
70 to 80 "	69.30	45.69			4658	1425
Over 80 "	26.21	19.69				

MORTALITY FROM TUBERCULOSIS TO EACH 10,000 OF LIVING POPULATION AT DIFFERENT AGES.



The solid lines indicate the male, the broken lines the female sex. The thickness of the lines is determined by the number of years of life included in a group.

per thousand who are wage-earners, mostly in factories and workshops. Among girls, there are only 667 per thousand, of whom 215 are employed about the house.

The number of infections reveals itself approximately in the mortality rate of the third succeeding year. The influence of factories and workshops and, in general, of the association of strangers becomes constantly more prominent, and after the twentieth year the mortality among males outstrips that among females, and advances progressively. The mortality among females also rises, but with far less rapidity, both because the circle of contact with outsiders is more narrow, and also because the wage-earning function is of far less significance.

Among cattle, on the other hand, the mortality is greater among the females—the cows. According to Röckl, the statistics of the slaughter-houses are as follows: 201,570 oxen and bulls, 6474, or 3.2 per cent., tuberculous; 178,749 cows, 12,314, or 6.9 per cent., tuberculous. Evidently this depends on the fact that cows are more generally kept in stables, as milk-providers, while oxen, as draught animals, are more constantly at work in the open.

Between the ages of sixty and seventy, the wage-earning capacity diminishes noticeably among men. The mortality from tuberculosis, nevertheless, continues to be high, especially in the first years of this period, because all of the tuberculoses acquired during the previous decade are transferred into this. A second important factor is the tendency of senile tuberculosis to run a chronic course, which tends to swell the mortality of old age.

After the age of seventy the individual tends to become more and more confined and isolated, and the mortality correspondingly sinks. After the age of eighty, the mortality is on a par with that of the first two years of life, and with that of the beginning of the twenties among women, just as the conditions of life, also, approximate to those of childhood, with their narrow confinement to the home and family.

It was formerly thought that the ages of twenty to forty were especially subject to the ravages of the disease. This idea resulted from the method of comparing the mortality from tuberculosis with the total mortality from all causes, which is a statistical blunder, and also from the fact that the data were generally gathered from hospitals. All sorts of theories were constructed to account for the supposed idiosyncrasy of this period of life. The hospitals are generally the resort of younger persons, especially in so chronic and helpless a disease as tuberculosis. Thus, the general hospitals of Prussia in 1885 presented the following conditions:

Age.	Percentage of the Total Number of Patients.	Tuberculosis, Hemoptysis, and Consumption.	
		Treated.	Died.
0 to 10 years	7.3	352	222
10 " 20 "	17.7	1,605	661
20 " 30 "	28.0	4,735	1,973
30 " 40 "	17.3	3,949	2,047
40 " 50 "	13.3	2,680	1,428
50 " 60 "	8.4	1,775	879
Over 60 "	8.0	995	651
Unknown		288	83
Total	100.0	16,379	7,944

For the same reason the material of the pathological institutes does not afford a measure of the conditions generally prevalent (see page 249). As an actual fact, this supposedly "predisposed period of life" shows only a low rate of mortality from tuberculosis.

The statistics above formulated by me (page 280) may be accepted with confidence, since they represent an average of sixteen years in a population of 27,000,000. Analogous conditions are found in other countries—Bavaria, Saxony, Norway (Larsen in Christiania). I fail to understand how certain authors can go on simply ignoring this mode of reckoning, or can venture to oppose it with statistics based upon a few hundred observations.

INFLUENCE OF POPULATION, SOCIAL CONDITIONS, VOCATION, AND CLIMATE UPON INFECTION.

It is characteristic of tuberculosis, as a contagious disease, that it is in direct ratio to the density of the population. A fair criterion of this density is the number of inhabitants per square kilometer of territory. Thus, in East and West Prussia, in which there are about 53 and 56 inhabitants respectively per square kilometer, the mortality from tuberculosis ranges from 15 to 21 to each 10,000 living beings in the various territorial subdivisions. In Westphalia and in the Rhine provinces the density is expressed by 120 to 175 respectively, and the mortality ranges from 33 to 50 per 10,000. This criterion is not always reliable, inasmuch as the density of population per square kilometer does not always express the degree of crowding within the same area. Moreover, there are many other conditions which serve in part to neutralize this single factor.

In the same way, the danger of infection is very much increased by unsanitary social conditions. Thus, in large cities it very often happens that four or six or even more persons are crowded together into one room. It was formerly thought that there was a considerable difference between the population of cities and of the country in the ratio of mortality. This difference is by no means constant. The life in the open air affords, of course, a certain guarantee against infection. On the other hand, the conditions of the dwelling-houses often counterbalances this advantage. The people live in narrow, dark, low rooms, and the small windows are kept constantly closed. It is possible, also, that association with tuberculous cattle may tend partially to increase the mortality in the country districts.

Vocation plays a considerable rôle in the spread of the disease. All occupations which are carried on in closed rooms are a source of far greater danger than those which are plied in the open air. The danger is increased by the fact that the larger the number of men associated in the work, the greater is the likelihood of tuberculosis in at least a few of their number, who then serve as a source of contagion.

Office employees, salespeople, and waiters contribute very largely to the mortality from phthisis; while coachmen, policemen, and street-cleaners (Author) fall below their proper quota. The danger becomes even greater if the business of the individual exposes him to much dust, if the sputum of his neighbors gets a chance to dry and become disseminated in the air. The finer the dust, the greater the danger; compare the work of carpenters and of porcelain-workers. If the dust is kept moist, the danger of dissemination is held in abeyance. The various qualities of the dust are, also, of much importance—its weight, its hygroscopic power, its contour. Sharp particles of stone tend to wound the epithelia, and so facilitate invasion by the tubercle bacillus (metal-grinders, stone-masons, etc.).

The character of the factory is of great importance. In small, low, and especially dark rooms there are many more and much more virulent bacilli in small space than in large, high rooms, especially such as are well lighted and ventilated. Inasmuch as the danger of infection corresponds very largely to the width of the circle in which the infected individual moves, and diminishes progressively toward the periphery of that circle, much depends on the degree of crowding in the workshops. If there is continual disturbance, the danger of dust dissemination is increased. If the cleaning-up is done during working hours, the workman is, naturally, more exposed to the inhalation of bacteria-laden dust than if it is finished so long before that the dust has had time to settle.

In many vocations the employees live together in large rooms (bakers); in others, they sleep in the workshop; in others, again, away from the factory. All these circumstances are factors of great importance. The relatively favorable conditions which surround the country laborer are neutralized by the fact that they live in shockingly crowded quarters.

The effect of overcrowding varies considerably with the climate, the geographical situation, and the season of the year. The colder the temperature, the greater is the tendency to remain indoors, to close the doors and windows, and thus to retain the dust. Excessive heat and great humidity act in the same manner. To a certain extent increased humidity tends to prevent the drying and pulverization of sputum, while windy conditions increase the danger. The sunlight exercises a marked influence upon the vitality of the bacteria. The interaction of these several factors is extremely complex, so that it is not possible to describe any one particular climate as the one most or least favorable to the development of the tubercle bacillus.

Everything depends on the combination of the various factors. A number of observations seem to indicate, for example, that coal-miners are noticeably free from consumption, notwithstanding the constant inhalation of coal-dust. It was customary, at one time, to attribute curative properties to coal-dust, and to recommend the mining places as health resorts for pulmonary invalids. (Schlockow, Valat, Desmarquette, Hervierk, Rimbault). The life of miners is spent largely under the most unsanitary conditions. A great part of their time is passed within the bowels of the earth, in narrow passageways, the walls of which are covered with moisture, non-porous, and most unfavorable to the circulation of air. Shut off from the sunlight, they labor by the uncertain light of a flickering oil-lamp, in an atmosphere poor in oxygen and laden with carbon dioxid, and polluted by the decomposition of the excreta of men and animals. When they leave the mine, they are exposed to a great and sudden change of temperature. Thus they are, therefore, subject to all those conditions which are generally considered to favor tuberculosis. And yet there is the strikingly low sick-rate: What becomes of the "decisive rôle of predisposition"? From the standpoint of infection, it is not difficult to explain this condition. The amount of moisture in these subterranean atmospheres approaches the saturation point, and renders the desiccation and dissemination of sputum impossible (see page 101).

It is possible that the coal-dust possesses a slight disinfecting power, but the essential cause of the apparent immunity certainly lies in the humidity. The following experiment of mine illustrates this fact: I kept fifteen animals in a small room, and subjected them for two weeks to the inhalation of carbon particles from a smoky lamp for several hours a day. In the third week I exposed the same animals to the inhalation of dust. Six to nine weeks later I killed the animals. Although the lungs and the bronchial glands were densely permeated by carbon particles, there were also extensive tuberculous foci, which stood out sharply in the surrounding black. In view of all the facts which have been adduced, I believe the conclusion is justifiable that contagion is by far the most potent factor in the dissemination of tuberculosis. Inasmuch, however, as certain physicians are inclined to regard heredity as the essential condition, the basis of this latter theory also will be exposed in the following chapter.

CHAPTER VI.

HEREDITY.

It is universally conceded that children of tuberculous parents frequently (though by no means regularly) become tuberculous. This fact has led many authors to ascribe to heredity a dominating influence in the etiology of this disease. Some of them, Baumgarten being the chief exponent of the theory, believe that such children are born with bacilli, whereas the majority merely assume that a certain predisposition is transmitted.

TRANSMISSION OF THE BACILLUS.

The transmission of the bacillus must be differentiated into a germinative (infection of the sperma or ovum during copulation) and an intrauterine or placental infection.

GERMINATIVE TRANSMISSION.

Tubercle Bacilli in the Sperma.—The germinative transmission through a tuberculous father necessarily presupposes the presence of tubercle bacilli in the semen. This does occur in the rare cases of urogenital tuberculosis. But what are the aspects of the problem if the urogenital system is healthy? Jani claims that he found tubercle bacilli (isolated?) in the healthy testicle in five persons out of eight who died of pulmonary tuberculosis.

Sirena and Pernice observed tuberculosis in dogs after injecting the semen from the seminal vesicles of a tuberculous individual, and Ziegler reviews similar results of Solles and Foà, which were not accessible to me in the original.

Furthermore, Spano narrates the striking result that in six cases of phthisis he demonstrated tubercle bacilli in specimens taken five times from the seminal vesicles and once from the testicle, partly by inoculation, partly by culture (?), partly microscopically.

Jäckh succeeded in demonstrating tubercle bacilli in the seminal vesicles and testicular secretions in two cases of advanced pulmonary phthisis with miliary tuberculosis of various viscera: viz., kidney, liver, parts of the prostate and peritoneum.

Aside from the fact that in Jani's cases microscopic examinations alone were made, by which the viability of the bacillus could not be proved, conclusions drawn from observations on corpses are by no means applicable to men who are alive and still sexually active. Furthermore, the normal condition of the testicle showed that the bacilli had become localized there only a short time, and consequently could only have reached the point toward the close of the patient's life. For the same reason the result of the examination of semen in miliary tuberculosis is no criterion.

The results obtained by Rohlff and Westermayer were entirely negative. The former inoculated the spermatic fluid from ten persons who died of phthisis into the anterior chamber of the eye of goats and rabbits; the latter implanted the morcellated testicles of fourteen similar cases (and, as I may add, the ovaries of the corpses) into the peritoneal cavity of rabbits. Both have proved by their negative results that if the urogenital system is healthy, the sperma of tuberculous patients is, with but rare exceptions, free from tubercle bacilli.

Walther carefully examined 161 sections of the testicle, 48 of the epididymis, and 63 of the prostate, from the bodies of 12 phthisical subjects, without finding a single bacillus. His inoculation experiments on animals with the same material from 9 corpses were also absolutely negative.

Dobroklonski examined the contents of the seminal vesicles in 25 who died of pulmonary tuberculosis, by means of smears and by inoculating guinea-pigs. Only in one case, in which a tuberculous epididymitis existed, was the result positive; in the other 24 it was negative. Here we might recall the cases of two children begotten of fathers with tuberculosis of the testis, who remained entirely well after nine months and two years respectively (Simmonds).

The more frequent presence of tubercle bacilli in the sperma would, moreover, give rise to a greater frequency of primary genital tuberculosis among the wives of the tuberculous and among prostitutes than experience shows to be the case. The theory of a transmission through the father lacks from the outset the *conditio sine quo non,* namely, the germ infection of the sperma.

Observations substantiating the theory of the transmission of a congenital tuberculosis through the father have not become available up to the present time. The case reported by Sarwey-Baumgarten—a focus of cheesy degeneration in the upper cervical vertebræ of a stillborn child—can in nowise be cited as a proof. The examination for tubercle bacilli was negative; the results of the inoculation experiments were very doubtful, and the histological findings of giant cells admit of a confusion with syphilis, in which (*e. g.*, gummata of the liver, Schmorl and Kockel) giant cells are also found. Moreover, the fact that the father also suffered from continued cough with viscid expectoration admits of various interpretations.

Animal Experiments.—The conditions of germinative transmission through the sperma would be more favorable in the guinea-pig than in the man, as the tubercular infection becomes more rapidly generalized in the former. The experiments of Landouzy and Martin, on account of their faulty technic, and as Rohlff, Baumgarten, and Gärtner have already maintained, can in no way be considered as influencing the question.*

Cavagnis, by inoculating the testicle of a tuberculous rabbit, and Gärtner, with artificially ejaculated semen of tuberculous guinea-pigs, were able to produce tuberculosis in five of thirty-two tests. Gärtner succeeded still more frequently (in about 50 per cent.) in finding the semen tuberculous when the testicles had been directly infected.

To secure the most favorable conditions for a germinative transmission, Gärtner injected tubercle bacilli into the testicles of 22 rabbits and 21 guinea-pigs and mated them with 65 females, of which 59 were healthy. The fetuses and young ones of these (29 rabbits and 45 guinea-pigs) in no case showed any tuberculosis (except one case of tuberculosis acquired later on through food).

The author was just as unsuccessful in demonstrating tuberculosis, either microscopically or by cultures, in 32 fetuses and young ones bred from guinea-pigs which had been inoculated in the testis. The negative result is all the more important because the females (9 out of 59 rabbits, and 5 out of 65 guinea-pigs of Gärtner, and one out of 28 guinea-pigs of the author) acquired genital tuberculosis through coitus. If, then, a germinative transmission has failed here, under the most favorable conditions conceivable, the assumption of such a theory for man absolutely lacks foundation.

Clinical data of men and animals (*e. g.*, Johne), derived from cases in which the progeny of an evidently tuberculous father also became tuberculous, are open to so many sources of error (extra-uterine infection) that they are entirely worthless as scientific contributions to the question.

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* By mistake these authors inoculated instead of the sperma of guinea-pigs, a secretion which serves to form the vaginal plug.

[Friedmann* succeeded in transmitting tubercle bacilli to the fetus through the semen. He injected a suspension of tubercle bacilli into the vaginæ of rabbits immediately after coitus. After six days the animals were killed, and the organs of the embryos contained tubercle bacilli. This is a striking and valuable observation, and proves by experimentation the possibility of direct transmission of the infection by the semen.—Ed.]

Tubercle Bacilli in the Ovum.—Against a germinative transmission Virchow had already raised the clinical objection that an egg invaded by and germinating under the influence of the tubercle bacillus retained its developmental properties and matured in normal fashion. Maffucci, and later on Baumgarten, endeavored to meet this objection by inoculating hen's eggs with the bacillus of avian tuberculosis and hatching them.

From eighteen eggs Maffucci obtained nine chicks, all delicate and small. Of these, two which died on the twentieth and thirty-second days showed only microscopically, but those dying on the fortieth, forty-seventh, and seventy-eighth days and after four and one-half months showed macroscopically as well an evident tuberculous degeneration. Baumgarten from twelve inoculated eggs obtained two chicks, which on their death, after four and four and one-half months respectively, proved to be tuberculous.

It is very clear that it is inadmissible to compare a bird's egg with the fundamentally different ovum of the mammal. Moreover, it is inadmissible to put this inoculation of the white or yolk of a hen's egg (which at the most corresponds to a placental infection) on the same plane with the germinative transmission in man, which process could only be imitated by an infection of the germinative area. No tubercle bacilli have been found thus far in the ovary.

PLACENTAL INFECTION.

The theory of a placental infection rests on a firmer basis. Though, as is well known, the maternal circulation is entirely separated from the fetal circulation, and the placenta forms an impenetrable filter for corpuscular elements, it has been shown that in acute infectious diseases (viz., variola, typhus, anthrax, cholera, measles, scarlet fever), in exceptionally rare cases and under conditions which we cannot at present control (perhaps a lesion of the placental vessels caused by the high fever, defects in the epithelium and chorionic villi, hemorrhages, etc.), the intervening wall is broken down and the bacteria circulating in the maternal blood reach the fetal organism.

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* Deut. med. Woch., Feb. 28, 1901.

An intrauterine infection in any one case is proved conclusively only, then, if tubercular changes in the fetus or newly born are noted either immediately or shortly after birth, so that a post-partum infection can be excluded by their location and degree of development. Otherwise we are not justified in denying an extrauterine infection, since it is precisely during the first few weeks after birth (especially if the mother be tuberculous) that the opportunities for infection are manifold.

The ease with which congenital syphilis may be confused with tuberculosis, to which Virchow has already alluded, as well as the occurrence of pseudo-tuberculous changes, which completely resemble tuberculosis macroscopically (such a case has been described by Henle in newly born twins), require absolutely the demonstration of the tubercle bacilli. It is for this reason that the older communications concerning congenital tuberculosis must be accepted with great caution.

[Heitz* took the liver of a six-months' fetus from a woman dead of consumption, inoculated portions of it into guinea-pigs, producing tuberculosis. He also found tubercle bacilli in the fetal liver.—Ed.]

Clinical and Pathological Observations.—The following observations on congenital tuberculosis were made by Charrin in 1873. The seven and one-half months' fetus of a consumptive died on the third day after delivery and had widely disseminated tuberculosis of the abdominal organs, with but few tubercles in the lung.

Berti noticed in the child of a consumptive which died on the ninth day after delivery two small cavities with cheesy degeneration in the right lower lobe. Nothing is mentioned about the other viscera.

Merkel, in 1875, observed a mother with cavities and miliary tuberculosis of the lung who died two days after giving birth to a child with a tumor of the hard palate the size of a pea which underwent cheesy degeneration. The tumor was accompanied by caseous cervical glands and cheesy focus in the left hip. The child died.

Jacobi published in 1892 a case observed in 1861. The seven months' fetus of a tuberculous mother had tubercles of the liver, spleen, pleura, and peritoneum.

Sabouraud, in the liver and spleen of a child that died eleven days after birth (the mother dying two months after labor), found numerous tubercles 2 mm. in diameter and containing tubercle bacilli.

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* Revue de la Tuberculose, 1903, p. 271.

Lannelongue, in 1005 cases of surgical tuberculosis between the ages of ten and fifteen, found three which, with considerable likelihood, could be traced to a congenital tuberculosis; a tuberculous osteoarthritis of the knee, originating on the fifteenth day after birth and accompanied by tuberculous abscesses; a case of tuberculous abscess of the tarsus over the region of the malleolus in a three weeks' old child, and a tuberculous osteitis in a child sixteen days old.

Furthermore, Rindfleisch has reported a case of a child, eight days old, with cheesy pneumonia and large cheesy nodules in the liver; the mother had acute phthisis.

To these should be added a case of syphilis with congenital tuberculosis (dead thirty-one days after delivery) reported by Hochsinger. Two other cases of Hochsinger (which died respectively in the sixth and sixteenth week after delivery) are not absolutely free from objections.

Further, Honl observed a fifteen days' old child with foci in the liver and spleen: there were a small number in the lungs.

Bugge, in the eight months' old fetus (dead thirty hours after delivery) of a mother suffering from generalized tuberculosis and dying shortly after, found tubercle bacilli both in the blood of the umbilical veins and also lying free in the lumen of a vessel in sections of the liver.

Bolognesi gives inexact and partly contradictory statements.

Doléris and Bourges describe an extremely doubtful case of a five weeks' old child.

Auché and Chambrelent observed a woman with advanced tuberculosis who died three days after the premature delivery of a seven months' fetus; there were numerous cheesy tubercles in the placenta. At the autopsy on the child, which died twenty-six days after delivery, there were found tuberculous nodules in the liver, spleen, lung, and right endocardium.

By inoculating portions of the fetal organs, especially the liver, spleen, etc., into suitable animals, it was possible to exclude any doubt that isolated bacilli, which as yet had produced no anatomical changes, were present in the fetuses in question.

More will be said later on concerning the earliest experiments made on this subject by Landouzy and Martin.

Schmorl and Birch-Hirschfeld (contributing the first certain case in man on record) found tubercle bacilli both in yellow foci of the placenta of a gravid girl who died of miliary tuberculosis, and also in the lumen of liver-capillaries of the seven months' fetus. The apparently normal liver, kidney, etc., proved to be tuberculous on inoculation.

Armanni produced tuberculosis in animals with portions of the organs (spleen, liver, brain) from the fetus of a woman who died of tuberculosis.

Lehmann found numerous tuberculous and cheesy foci in the child of a consumptive which died twenty-four hours after birth.

Thiercelin and Londe observed two children the mother of which died soon after labor from pulmonary and intestinal tuberculosis (no autopsy). In the first child, which died after four days, numerous tubercle bacilli were found in the spleen, liver, and kidney; there were no macroscopic changes. A guinea-pig which was inoculated with blood from the umbilical vein died from general tuberculosis. There was no autopsy on the second child, but portions of the placenta produced tuberculosis in a guinea-pig.

Additional positive results by means of inoculation were obtained by Herrgott and Haushalter (liquor amnii from a woman who died in the sixth month of pregnancy from phthisis); by Londe (blood from the umbilical vein and apparently healthy organs of three fetuses from tuberculous mothers); and by Aviragnet and Préfontaine (portions of the placenta of a gravid woman, who died in the seventh month, and the liver of the fetus).

Bar and Rénon inoculated the placental blood of the umbilical vein five times into guinea-pigs, three times with negative and twice with positive results. In the latter cases the mothers were in the last stages of phthisis.

Similar observations are recorded in the literature of animal medicine. Indeed, we are indebted to the latter, or rather to Johne, for the first conclusive demonstration of an intrauterine transmigration of tubercle bacilli. In the case in question the eight months' fetus of a tuberculous cow had tubercles of the lungs and the bronchial glands, but not markedly in the liver.

Two cases (Malvoz and Brouwier) follow: The eight months' old fetus of a cow with generalized tuberculosis showed numerous tubercles in the liver, the glands of the hilus of the liver, and the bronchial glands, the lung remaining entirely free. The second case is not as conclusive: a six weeks' old calf had two cheesy foci in the liver, with cheesy glands at the hilus and cheesy bronchial glands. The lungs were free.

Czokor observed a fetus with cheesy foci in the hepatoduodenal ligament of a cow suffering from general tuberculosis.

Three further cases by Bang: A fetus with cheesy gland the size of a walnut at the hilus of the liver; a two days' old calf with cheesy mesenteric and bronchial glands, and miliary tubercles of the lung and liver. A fifteen days' old calf with a gland the size of a walnut at the liver hilus, submiliary tubercles of the liver, cheesy mesenteric, mediastinal, and bronchial glands, etc.

McFadyean also observed a five days' old calf with cheesy foci in the liver and portal glands.

Siegen found tubercle bacilli in 32 calves under fourteen days old and in six fetuses. In one case the placenta of a tuberculous cow showed tuberculous changes.

Lungwitz (also Kockel) observed two cases of fetal tuberculosis in 200 cases of bovine tuberculosis examined in the Dresden slaughterhouse. The infection appeared to originate from the porta. In the first case, in addition to a widespread tuberculosis of various organs, there was tuberculosis of the uterus. In this case the maternal villi lying immediately beneath the chorion and also in part the fetal villi were destroyed and converted into a mass consisting of pus cells and nuclear detritus. Numerous tubercle bacilli were found in the tuberculous foci of the mucous membrane and in the masses of detritus, but only a few in the substance of the fetal villi. In the second case the findings were similar, both as regards mother and fetus.

Nocard found numerous tubercle bacilli in the swollen glands at the liver hilus and on the surface of the liver of a seven months' fetal calf; the tuberculous cow showed tuberculous changes in the cotyledons (tubercle bacilli).

Observations on congenital tuberculosis have been made, in addition, by Grancher, Köhler, Misselwitz, Bang, Bayersdörfer, Beckers, Ruser, Baerlund, Czokor, Galtier, Chauveau, Bucher, and by Lohoff in a three weeks' old calf; their accounts, however, have been somewhat inexact.

[Schlueter* has collected twelve well-authenticated cases of congenital tuberculosis in man; seventy cases in animals. He concludes that it is a rare occurrence, though rather more common than has been supposed; but of course it is not a considerable element in the causation of phthisis. He says that the commonest path of infection is by way of the placenta; that infection of the ovum or infection by the semen of the father is exceedingly rare.—Ed.]

Experimental Work.—The small number of fetuses from tuberculous mothers accessible to investigation under natural conditions induced observers to investigate the question of heredity experimentally. Females were therefore inoculated with tubercle bacilli, either before or after conception, and the progeny examined.

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* Die Fötale Tuberk. Infekt., Leipzig u. Wien., 1902.

The first positive assertion that the fetuses of experimentally infected mothers became tuberculous was obtained by Landouzy and Martin, and de Renzi. These so frequently quoted experiments are no less free from objections than the findings of Koubasoff, who claimed to have demonstrated the migration of the bacilli microscopically. (Consult Gärtner's well-founded criticism of the same, page 128 and pp. 187–8; also Straus, pp. 545–547.)

Cavagnis (1885–1886) produced tuberculosis by inoculating the spleen of a guinea-pig born of a tuberculous female.

Gärtner alone has succeeded by means of intraperitoneal, intravenous, or intratracheal injections into pregnant females in producing progeny which in about 5 to 10 per cent. of the cases proved to be congenitally tuberculous. He made use of an enormous number of animals.

Gärtner injected 0.001 to 0.002 cc. of a pure culture in suspension into the peritoneal cavities of 102 white mice, of which 72 were females. This seemed to offer the most favorable condition for a direct infection of the ovum. He obtained 19 suitable litters, with 96 young ones. They were ground to a pulp in toto, and generally three at a time were inoculated into the peritoneal cavity of guinea-pigs. Out of the 19 litters it was found that in two cases the ovum had become infected.

To insure analogous conditions for the development of a miliary tuberculosis, he injected 0.5 to 2 cc. of a culture of tubercle bacilli into the ear-veins of ten sound rabbits. Of the 51 fetuses or young ones which he secured, 25 were dead or premature. Of these 51, five (*i. e.,* 10 per cent.) were tuberculous. The entire litter was never tuberculous; at the most, two or three young ones.

With a view of studying the most common form of tuberculosis in man, namely, pulmonary phthisis, Gärtner injected a drop of a pure culture of tubercle bacilli into the trachea of each of 64 female mice. Several died immediately, but he secured 18 useful litters numbering 74 young ones. By inoculating these on 39 guinea-pigs, he found that 9 of the 18 litters contained tuberculous young ones. With similar inoculations on 28 females, carried on at a later time, Gärtner secured only one tuberculous young one.

Far greater is the number of authors who were unable to demonstrate tuberculosis in the products of conception from tuberculous mothers.

Straus repeatedly inoculated the organs of a woman with advanced phthisis into guinea-pigs with entirely negative results.

Von Leyden (1884) also was unable to produce an inoculation tuberculosis with the organs (liver, spleen, lungs) of a child born of a tuberculous mother who died shortly after the delivery, nor with the organs of a fetus from a tuberculous guinea-pig.

Von Nocard (1885) inoculated the organs of 32 fetuses obtained from four tuberculous rabbits and from eight tuberculous guinea-pigs into 32 guinea-pigs. Results negative.

Wolff (1886) was unable to demonstrate tuberculous changes in 42 fetuses of rabbits and guinea-pigs from tuberculous mothers either with the naked eye or under the microscope. In one case he secured a positive result by inoculation.

Jaquet in several human fetuses of tuberculous mothers was able to find tubercle bacilli microscopically.

Further unsuccessful inoculations were made by Galtier with the organs of the young of nine tuberculous guinea-pigs, as well as with the organs of the calf of a tuberculous cow.

Similar results were obtained by Grancher and Straus with the liver, spleen, and lungs of fetuses (14 inoculations) from nine tuberculous female guinea-pigs; the remaining progeny of these females were killed after five months, one year, fifteen and sixteen months, respectively, but failed to show any trace of tuberculosis at the autopsy.

We are indebted to Sanchez Toledo for an especially painstaking investigation. He injected 1 cc. of an emulsion rich in bacilli into the veins of 15 female guinea-pigs, death ensuing regularly after fifteen to twenty days. Their progeny—in all, 25 fetuses—microscopically showed no bacilli in the liver, nor could cultures be obtained either from the blood or by inoculation. The inoculated animals remained alive more than six months and were free from tubercles. The same result was obtained with 17 fetuses of eleven female guinea-pigs which had been inoculated in the thorax, as well as with 13 fetuses of nine animals inoculated subcutaneously with sputum. To sum up, 65 fetuses from 32 tuberculous females proved to be non-tuberculous.

Vignal inoculated the liver and spleen of 11 human fetuses and still-births of phthisical mothers, as well as 17 placentæ of tuberculous women, and lastly the organs of 11 small guinea-pigs born of tuberculous mothers. Some of the inoculated animals lived upwards of five months; none became tuberculous.

Even Baumgarten,* who is the strongest defender of the theory of heredity, was unable, in spite of numerous attempts, to demonstrate tubercle bacilli, either microscopically or by inoculation, in the organs either of the embryos or of the newly born, obtained by mating tuberculously infected rabbits.

Troissier inoculated the liver and lungs of three still-births from phthisical mothers. Result negative.

The author also made a series of experiments on this subject in the years 1888–89.

(*a*) In 96 animals born of and nursed by tuberculous mothers I was unable in the course of five weeks' observation to detect any deviation from the normal development, let alone a tuberculosis.

(*b*) Furthermore, portions of the liver (that being the organ chiefly affected in transmission) taken from 25 still-births of tuberculous females were inoculated on other animals. In no case did the liver prove tuberculous.

(*c*) To meet the objection that bacilli might have been deposited in other parts of the fetus, I ground up entire embryos, taken at an early stage of development from tuberculous mothers, and inoculated all parts (in all, from 96 embryos) on 114 animals. Even in this case none of the inoculated animals became tuberculous.

(*d*) Twelve embryos obtained from females suffering from an inoculated genital tuberculosis were ground up and all parts inoculated; also portions of the liver of four young ones born of a mother suffering from genital tuberculosis. There also the results were all negative. To sum up: out of 233 products of conception, none was tuberculous.

Criticism.—If we collect all the facts which speak for a placental transmission, we have in all about 20 cases submitted to us in man. Certain of these cases indicate with certainty the possibility of a placental transmission; a considerable number of others, however, are of doubtful significance, so that they cannot be accepted as unqualified evidence.

Animal medicine presents a much greater number of cases, and it is even possible that the frequency of congenital tuberculosis in calves has been underestimated, since, owing to the conduct of business in the slaughter-houses, the necessary time, and probably also the interest, was lacking for such researches. Since attention has been directed to it, the number of such cases has considerably increased; whereas—*e. g.*, in Kiel—formerly only nine unsuckled calves were found to be tuberculous within eight and one-fourth years, Klepp was able within the short time of five months to discover 26 cases of tuberculosis among 4086 unsuckled calves (0.64 per cent.), and later on in one month, 10 among 847, or 1.18 per cent. This shows also that even with the most accurate observation congenital tuberculosis in animals is a great rarity.

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* Concerning the single case in which a nodule the size of a cherry was found in the liver of such a rabbit, Baumgarten himself said that the proof was entirely insufficient.

As regards the experimental proofs, Gärtner has furnished undoubted evidence that in the species used (rabbits and white mice) a migration of tubercle bacilli from the mother to the ovum is possible under certain conditions. We must not overlook the fact that these animals were practically flooded with tubercle bacilli. It must be borne in mind that to duplicate Gärtner's methods of infection a gravid woman weighing 70 kg. would have to be inoculated with 350 gm. of a strong infusion of tubercle bacilli in the trachea, or 35 to 140 into the circulation, or about ½ to 1½ liters into the abdominal cavity. A migration under such markedly abnormal conditions is not astonishing, and does not entitle us to draw deductions offhand as to the natural conditions in man. The researches of Gärtner are no just criterion, for the further reason that they were not cases of localized pulmonary tuberculosis, but of generalized tuberculosis, in parts originating from the lung.

These results are to be contrasted with the reports of the other nine authors, who among more than 340 fetuses taken from animals suffering with advanced tuberculosis only twice (Wolff and Cavagnis) obtained positive proof of the transmission of the disease. The experiments do, indeed, prove the possibility of a placental transmission, but, above all, its rarity, since, even under extremely favorable circumstances,—as in miliary tuberculosis,—such a transmission either does not take place at all, or takes place only under a set of conditions which finds no parallel in life.

If, then, we consider the two questions, first, whether placental transmission is possible; and, second, whether it occurs so frequently as to constitute the principal cause of dissemination in tuberculosis, we must answer the former unconditionally in the affirmative, but the latter absolutely in the negative.

On the one hand, if one-seventh of all human beings die of tuberculosis, and in addition a not inconsiderable number have latent foci, then heredity, as the exclusive or almost exclusive method of transmission (as Baumgarten and others would have it), would require that one-seventh of all human beings carried the germ within them at birth.

We have the assurance of the most reliable pathologists, such as Virchow, that in their experience—extending over decades—they have never seen a genuine case of congenital tuberculosis; or they designate such a case as a rarity which has occurred only in connection with uterine tuberculosis in the mother.

In Prussia alone, with a population of 30,000,000, there are yearly 40,000 still-births and 70,000 deaths of children under one month. If, then, of these millions of children under one month, one-seventh contained the germ of tuberculosis, in relation to these enormous numbers what do the 20 cases observed in man signify, and these 20 observations, too, not entirely above reproach? These figures do not overshoot the mark; indeed, they embrace only a minority of the cases—those on which autopsies were performed in pathological institutes, hospitals, and lying-in institutions, where the attention of pathologists has for years been specifically directed toward the point at issue.

It would be directly contrary to facts if, in view of such data as these, one should still attempt to maintain the doctrine that congenital transmission is the exclusive or even the most frequent mode of dissemination. Palpably, we can only conclude that it may occur exceptionally or under extraordinary conditions.

Conditions Governing the Transmission of the Tubercle Bacilli.—The peculiar conditions governing this probably consist in a rupture of the placenta, which normally forms a firm barrier between the maternal and fetal circulations, and the simultaneous appearance of bacilli at the point of rupture.

Both of these conditions would be very easily fulfilled if a tuberculous focus were located in the placenta. Possibly both might also be realized if, through such causes as high fever or the action of toxins, a disintegration of placental villi should occur, and the maternal circulation was flooded with bacilli at the same time, so that a few would reach the spot.

Tuberculous foci in the human placenta are, according to our present knowledge upon this subject, a rare occurrence. For some time it was held that this organ was immune to bacilli. The mere finding of bacilli and the positive results from inoculation which several authors have reported are no proof of tuberculous changes in the tissues. True placental tuberculosis has been described by Lehmann in a case of extensive miliary tuberculosis, and by Schmorl and Kockel in three women, two of whom died of acute miliary tuberculosis and one of chronic pulmonary phthisis.

Placental tuberculosis is more frequent in cattle. Siegen, Kockel and Lungwitz, and Nocard report such observations. This explains that congenital tuberculosis has been found more frequently in animals than in man. It shows, too, that it would be incorrect to base deductions for man upon the dissemination of tuberculosis among unsuckled calves.

Placental tuberculosis occurs more frequently in cattle for the reason, probably, that tuberculosis of the uterus as well as pelvic tuberculosis (which is rare in human beings), according to Kockel and Lungwitz, very frequently occur in cows even in the absence of a generalized tuberculosis.

In man, as pathology has shown, tuberculous foci of the placenta are rare, even though the circulation is flooded with bacilli (miliary tuberculosis), though numerous bacilli have been deposited in all the viscera and tubercle formation has occurred. Schmorl and Kockel, to whom we are indebted for the first observation of a placental tuberculosis, call particular attention to this fact; only I would not attribute the cause, as these authors do, to a minimal predisposition of these organs, but to the increased diameter of the vessels, which favors the deposition and retention of circulating bacteria to a less degree than do narrow capillaries.

The few recorded cases of congenital tuberculosis are almost invariably associated with a localization of the tuberculous process in the placenta, so that the latter is probably a factor, if not the exclusive one, in determining this form of transmission.

But even when a tubercular focus has formed in the maternal placenta there are still many obstacles to the migration of the bacilli into the fetal circulation. Schmorl and Kockel, in their painstaking histological examinations of placental tuberculosis, call attention to the fact that the placental villi, even when entirely embedded in the tuberculous growth, for a long time retain their integrity almost, if not completely, intact, and are readily differentiated from the surrounding granulation tissue. "Even the identical villus on which the primary localization of the tubercle bacilli occurred, and which in consequence lacks its cellular sheath in places, remains for a long time unchanged. The tubercle bacilli may be ever so numerous in the tuberculous new-growth, yet within the villi surrounding this area we hardly ever find them." From this it appears that the villi offer great resistance to the passage of tubercle bacilli, and only gradually succumb.

If the villus itself finally becomes tuberculous, then, as we have repeatedly stated regarding the blood-vessels (see also chapter on Pathological Anatomy), and Schmorl and Kockel have also emphasized, a thrombosis and obstruction of the vessels occurs, which tends to prevent an entrance of the bacilli into the fetal vessels which still contain circulating blood.

From this condition of affairs we may conclude that the demonstration of bacilli in the placenta alone, either microscopically or by inoculation, proves nothing as to the transmission of bacilli to the fetus.

Aside from a placental tuberculosis, transmission is possible, as has been already mentioned, if the maternal and fetal vessels have suffered a solution of continuity under the influence of high fever or other factors, and if, at the same time, tubercle bacilli reach this spot.

Such solutions of continuity may be caused by a disease of the placenta entirely independent of the tuberculosis, by a trauma, by high temperature, and perhaps, also, by the concentration of toxin. As has been mentioned above, such lesions are often found in syphilis; it is explainable for this reason that in a syphilitic mother suffering at the same time from tuberculosis, avenues for the transmission of the latter disease are opened up by the former. We have a clinical example of this in the case cited by Hochsinger (vid. sup.). Such solutions of continuity in the placenta, judging from observations at hand, are found only exceptionally in tuberculosis.

But with this solution of continuity alone an intrauterine transmission would not be proved; it is essential that bacilli must reach this very place; in other words, the bacilli must circulate in the blood.

The case reported by Schmorl and Birch-Hirschfeld may serve as an example of the coexistence of both conditions. In the case in question the placenta, which was free from tuberculous changes, showed isolated hemorrhages and several infarcts on its uterine surface, in part directly beneath the chorion. The mother had died in an advanced stage of general tuberculosis; numerous tubercles were disseminated through the lung, spleen, liver, kidney, and adrenals, and the wall of the thoracic duct had been destroyed by a caseous gland, and crumbling cheesy masses lay in its dilated lumen. In transverse sections of the chorionic vessels there were found isolated bacilli among the red blood-cells. The condition that bacilli must circulate in the blood bars any comparison with syphilis, smallpox, or experimental anthrax. In infectious diseases of this kind the vascular system and all of the body-fluids are permeated with the contagion, so that a transmission to the fetal placenta is more readily accomplished. Moreover, the disease itself gives rise to lesions (hemorrhages of the placenta) which explain the path of the infection. But even in smallpox transmission is rather the exception as compared with the cases in which neither the fetus nor the embryo showed traces of the disease. Even in syphilis, the hereditary disease *par excellence,* women who become infected while pregnant, and show symptoms of a recent general infection at parturition, give birth to children without any symptoms of syphilis, either *intra vitam* or at autopsy if they happened to die from any other cause (Birch-Hirschfeld). With anthrax the extremely high proliferative powers of the bacilli, which by their rapid growth crowd all membranes asunder, add another factor; in spite of this, transmission occurs only in a fractional part of the cases.

In tuberculosis the situation is entirely different. Here bacilli are found abundantly only in acute miliary tuberculosis. But even if the vascular system is flooded with bacilli, the filtrating action of the placenta appears to suffice as a protection for the fetus, as the histological findings and the series of clinical observations previously mentioned have proved.

We see this exemplified in a case observed by Heller and cited by Rohlff, where, in spite of an advanced tuberculosis of the kidney, the ureter, and the uterus, and notwithstanding the fact that all the viscera and even the circulation were full of tubercle bacilli, no bacilli were found in the fetus. Similar case are reported by Weichselbaum and Birch-Hirschfeld, and experimental pathology (see page 294 seq.) is replete with such instances. Hagenbach reports a case of a child born of a phthisical mother in the agonal stage, which up to its fourteenth year (that being the limit of his observation) did not show any trace of tuberculosis or scrofula.

In chronic pulmonary tuberculosis, as numerous investigations indicate, when the blood is free from bacilli or only occasionally retains an isolated individual, transmission is still more difficult, if not impossible. Especially is this the case in those early stages of pulmonary tuberculosis which we encounter most frequently in parturient women. It is true that Arnold, Brissaud, and Toupet found minute tubercles, scarcely visible to the naked eye, in the liver of consumptives, and other authors have found tubercle bacilli in the blood and even in the muscles after death, or in the last stages of the disease. Frerichs also speaks of blood-infection in pulmonary phthisis, which occurs, however, in less than one-half the cases.

It is evident that in these cases the bacilli entered the blood or the organs only a short time previous to death. This is proved by the entire absence of anatomical changes, or their low grade of development if present, a pathological finding which, in view of the marked "predisposition" of the tissues in consumption, admits of no other explanation. The invasion, therefore, occurred in the terminal stage, and is probably in causal relation with the simultaneous resorption of proteins, as will be shown later on in connection with the causes of death.

The cases of congenital tuberculosis which could not be accounted for by a marked placental tuberculosis lacked in no recorded instance the etiological factor of the mother suffering from miliary tuberculosis (in one case of Schmorl and Kockel from advanced pulmonary tuberculosis) of such severity that death occurred either previous to parturition, during it, or shortly after. In no case, so far as I know, did the mother survive the birth of the child for more than a short time.

But even if an intrauterine transmigration of bacilli did occur more frequently in miliary and advanced tuberculosis, or even if it were the rule (which, judging from the facts adduced, is by no means the case), heredity would, nevertheless, play but a small part in the dissemination of tuberculosis.

How few of those 150,000 or at present 120,000 people dying yearly in Germany of tuberculosis are descended from mothers who as a result of miliary or advanced pulmonary tuberculosis died shortly after their labor! Such cases are rather exceptional.

Haupt, who is inclined to stretch the limitations of heredity to the utmost, was able to demonstrate a hereditary taint on the mother's side in only 143 out of 617 of his patients—less than one-fourth of the cases. His figures include not only those mothers who at parturition had suffered from miliary or advanced pulmonary tuberculosis, but also those who at any time, perhaps years or decades after the labor, suffered from tuberculosis, the majority of whom probably enjoyed the very best of health at the time of parturition.

Of the 751 mothers of my tuberculous patients, there died after the birth of the oldest tuberculous child: in the first quinquennium, 45—the cause of death being tuberculosis in 16, in 1 suspected, in 5 unknown; in the second quinquennium, 58 from tuberculosis, 19 suspected, from unknown cause 7. Of these mothers, 648 survived the labor for upwards of ten years, and consequently could not have been highly tuberculous at that time.

We cannot accept the theory that a notable percentage of the tuberculous have acquired the disease through an intrauterine infection; on the other hand, we can hardly doubt that mothers with miliary and advanced tuberculosis have given birth to children with bacilli more frequently than a record of 20 cases would seem to indicate.

In Saxony (I have found no statistics of other countries on this subject) 100 parturient women die annually within the first four weeks after labor from acute and chronic tuberculosis. It is evident that in these cases the disease must have been well advanced at parturition. From these figures we could estimate that in the whole of Germany there would be annually about 1400 lying-in women with advanced tuberculosis. We can unhestitatingly admit that a transmission of the bacillus has occurred with a fair number of their 1400 children. Even if these figures are insignificant when compared with the general extent and dissemination of the disease, they nevertheless represent a factor of importance in individual cases.

The Fate of the Congenitally Tuberculous.—What is the fate of such children with congenital tuberculosis? In one case the child lived three weeks, in another eight days. The remaining cases were not even full-term children, but fetuses of five to eight months, which were delivered by Cesarean section of the moribund or the dead.

If, exceptionally, a migration of bacilli to the fetus does occur, we must still assume that the simultaneous transmission of the diffusible tubercle-proteins from the maternal organism which is saturated with these toxins plays the important rôle, and that it is to them that these fetuses or children rapidly succumb.

In fact, all our present data admit of but one interpretation, namely, that a genuine infection speedily causes the death of the fetus. Not a single observation have we that such an infected fetus is able to carry on an extrauterine existence of several weeks' or months' duration, let alone tracing a tuberculosis of later years (and this is the important point in practice) to an intrauterine infection.

The observation that abortion or premature labor is not uncommon in advanced tuberculosis has also been made by veterinarians. Likewise, that the full-term fetuses of such mothers speedily die.

One important point calls for special mention. The fetuses which up to the present time have been examined and pronounced congenitally tuberculous have not all shown the macroscopically or microscopically demonstrable tuberculous changes in their viscera. It is only in a few that such foci were found. In the majority of the cases the bacilli have been found with the microscope either in the blood or in the hepatic vessels alone; and then only by inoculating the blood of the umbilical veins or of the viscera, especially the liver, could a tuberculosis be diagnosed. This evidently indicates that the infection of the fetus occurred shortly before the miscarriage or labor, perhaps even during the labor itself, possibly through a rupture of vessels from the increased pressure due to the uterine contractions.

It would be rather far-fetched to conclude from these facts that the fetal tissue possessed an increased power of resistance; reference will be made to this theory later on. These findings are rather analogous to those previously mentioned in autopsies on consumptives of organs macroscopically and microscopically intact, but containing bacilli, which we are forced to explain as cases of antemortem invasion.

Further Objections to the Theory of Heredity.—A number of other facts also cannot be reconciled with the assumption of a preponderating influence on the part of heredity. I allude particularly to—

The Mortality of Different Ages.—The assumption of a frequent congenital transmission is at variance with the facts relating to the frequency of tuberculosis at the different periods of life. For if this were true, we should expect the greatest frequency during childhood, and a diminution with increasing years, owing to the successive deaths of tuberculous individuals; whereas, in fact, the very opposite is the case.

I refer the reader to the table (see page 280) on the mortality from tuberculosis at different ages.

A differentiation according to months, which would be very valuable for the first year of life, we are unfortunately not able to determine from the general statistics. The table shows plainly, however, that in the first few years of life tuberculosis occurs with relative frequency for the reasons mentioned there, but decreases from the third year on. On the other hand, after the fifteenth year, up to which time only one-seventh of the deaths from tuberculosis have occurred, there is a progressive increase up to the sixtieth to the seventieth year, whereupon a decrease again commences.

On the basis of heredity we cannot explain these figures, whereas with extrauterine infection, as we have seen, the explanation is self-evident.

Tuberculosis is so typical in adults and older children that it is recognized even by the layman without difficulty. The figures furnished by the general statistics on mortality are, therefore, reliable in this respect. For early childhood, however, in which the clinical picture frequently is not so typical, I do not think that they can be considered trustworthy. For the sake of verification and completeness, I have subjoined the results of clinicians and pathologists:

Demme observed among 36,148 patients of the children's hospital, 1932, or 5.3 per cent., with tuberculosis.

Lannelongue has observed 1005 cases of external tuberculosis; of these, there occurred:

At 1 year	87*
" 2 years	144
" 3 years	107
" 4 years	108
" 5 years	99
" 6–10 years	299
" 11–15 years	125
	969 †

In Biedert's statistics on the autopsies of 1308 tuberculous children, there were:

Under 1 year	90, or 7	per cent.
1 to 5 years	628, or 48	"
5 to 10 years	358, or 27	"
10 to 15 years	232, or 18	"

The relation between deaths from tuberculosis and the mortality of children in general is shown in the following statistics:

Age.	Simmonds, Schwer and Bolz.			Müller.		
	Autopsies.	Tuberculous.		Autopsies.	Tuberculous.	
		Number.	Percentage.		Number.	Percentage.
0– 1 year	1438	64	4.5	49	3	6.1
1– 5 years	781	230	29.3	272	73	26.8
5–10 "	228	78	35.0	105	39	37.2
10–15 "	162	56	34.6	74	35	47.3
Totals	2609	428	16.4	500	150	30.0

In Müller's statistics children under one month are omitted, which accounts for his high figure (30 per cent.).

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* Some in the ninth and tenth week.

† As Gärtner has also observed, the addition gives the sum 969, instead of 1005 as it ought to be.

During the first few months tuberculosis practically does not occur.

Schwer found among 263 children between the ages of one day and one month, 0 tuberculous (0 per cent.); 123 children between the ages of one and two months, 1 tuberculous (0.8 per cent.); 144 children between the ages of two and six months, 15 tuberculous (10.4 per cent.); 160 children between the ages of six and twelve months, 28 tuberculous (17.5 per cent.).

Hutinel found in 118 autopsies on children, 4 tuberculous (less than three and one-half per cent.), the respective ages being forty-one days, two, six, and seven months. The younger ones had nodules in the lung, the two older ones pulmonary tuberculosis. Of the children that were one to two years old, one-third showed tuberculous lesions.

Hervieux in 996 autopsies on children found only 18 tuberculous under the age of two, 10 under one, and only two under three weeks.

Froebelius in 16,581 autopsies on children under two years found only 416 (45 per cent.) tuberculous, of which 3 were less than three weeks of age.

Queyrat found 11 tuberculous cases in 35 autopsies of children under two years, the youngest being three months.

Epstein in 200 autopsies on children, for the most part under six months, found 9 tuberculous, the ages varying from ten weeks to ten months.

Klebs calls attention to the fact that among the numerous cases in the foundling asylum at Prague, tuberculosis is found at the very earliest three weeks after birth.

According to Heller, of every 100 deaths in Kiel at the following ages, there died of tuberculosis, up to the first month, 0.0 per cent.; up to the second month, 0.83 per cent.; up to the sixth month, 11.3 per cent.; up to the twelfth month, 22.5 per cent.; up to the second year, 29.0 per cent., etc. Among 350 still-births he did not find a single case of tuberculosis.

Kossel found in 286 autopsies on children 22, varying in ages from two months to five years, who had died of tuberculosis.

Neumann reports from autopsies on 142 children the following:

0– 5	months	old,	among	36	tuberculous,	0	per cent.
6–12	"	"	"	33	"	7	"
1– 2	years	"	"	28	"	10	"
3– 5	"	"	"	18	"	13	"
6–10	"	"	"	16	"	12	"
11–14	"	"	"	11	"	5	"
				142		47	per cent.

With the kind permission of Professor Virchow, my assistant, Dr. Rothe, made excerpts from the autopsy records relating to children under five years of age. My compilation gives the following result:

	Still-births and 1 Day Old.	1 Day to 4 Weeks.	1 to 2 Months.	2 to 3 Months.	3 to 6 Months.	6 to 9 Months.	9 to 12 Months.	Total for First Year.	1 to 2 Years.	2 to 3 Years.	3 to 4 Years.	4 to 5 Years.	Total.
Number of autopsies	184	250	52	33	76	88	65	748	311	189	160	134	1542
Number with tuberculous changes. . .	—	—	—	2	8	15	18	43	83	56	51	30	263

Note.—One hundred and thirty-five children, of whom 32 had tuberculous foci, were excluded from the table, no age being given.

These figures demand careful study, since they are based on statistics of children's hospitals, the material of which varies greatly with the conditions for admission, and is, moreover, recruited from the poorest classes, among whom tuberculosis is more common than among those better situated. It must further be borne in mind that children even of the poorest classes are generally kept at home during acute diseases, in which death occurs quickly, and are brought to a hospital only when they require prolonged care (as in tuberculosis), so that tuberculosis appears to play a more important rôle than is warranted by the facts.

These figures do not give a correct picture of the frequency of tuberculosis at different ages, inasmuch as they are taken from a wrong point of view. Instead of comparing the number of consumptives with the living of the same age, they are compared either with one another or with the entire mortality statistics, disregarding in one case the unequal distribution of the living people of the same age, in the other the influence of factors entirely independent of tuberculosis, *e. g.*, an increased or diminished mortality from diphtheria. For this reason it is incorrect to quote these figures repeatedly and without criticism as the basis of new hypotheses.

From these figures we are only able to ascertain with certainty that tuberculosis practically does not occur in the first three or four weeks, and that it is very rare in the first months.

Analogous Data of Veterinary Medicine.—The important data on this subject, for which we are indebted to veterinary medicine, are in complete accord with the facts above cited.

A circular letter addressed by the author in 1889 to the principal abattoirs in Germany gave the following information, in some cases dating from the year 1881: Of 39,884 unsuckled calves, 2, or 0.005 per cent.; of 2,312,994 calves without stated ages, 178, or 0.008 per cent.; of 1,339,120 cattle, 35,154, or 2.63 per cent., were found to be tuberculous.

The statistics upon the distribution of bovine tuberculosis in Germany show, according to Röckl, that, as a rule, tuberculosis is rare in animals under one year and hardly comprises one per cent. of the cases reported. The frequency of tuberculosis increases directly with age; from the first to third years the percentage is about 10 times as great, from three to six years more than 30 times, and over six years more than 40 times, as great as for the first year.

In Prussia in the years 1894 and 1895 the department of agriculture reported that in the slaughter-houses there were slaughtered calves under six weeks, 1,950,704; cattle, 1,335,492. Of this number, 1314 calves, or 0.07 per cent., and 152,447 cattle, or 11.4 per cent., were tuberculous.

In Baden, during the year 1888–89, tuberculosis was found among the slaughtered cattle as follows: Calves, 0.004 per cent.; heifers, 0.42 per cent.; cows, 4.94 per cent.; oxen, 1.25 per cent.; bulls, 1.91 per cent.

In Saxony, where the inspection of meat is compulsory, the distribution of tuberculosis was as follows:

Of	120,490	calves	up to six weeks of age	3, or	0.002	per cent.
“	665	cattle	from six weeks to one year	1, “	0.15	“
“	6,328	“	“ 1–3 years of age	440, “	6.9	“
“	13,307	“	“ 3–6 “ “	1285, “	9.7	“
“	11,101	“	over six “ “	1881, “	16.9	“

We observe, therefore, in man and beast alike, exclusive of rare cases, that tuberculosis does not appear until after several weeks of extrauterine life; in other words, not until a time at which the possibility of a post-fetal infection must also be considered.

I scarcely need to explain that these opportunities for infection are particularly frequent in the early period after birth and during the first few years of life, since the child is then kept in close communication with the parents almost continually, especially with the tuberculous mother, and is, moreover, endangered by the exclusively milk diet. Is it not striking, as the Prussian and Bavarian statistics attest, that the frequency of tuberculosis in children of one to two years of age is approximately the same as for women from eighteen to twenty-eight years, the average period of child-bearing? As soon as the child has acquired a certain freedom of motion,—that is, from the third or fourth year on,—but especially after it is removed from the close circle of the family through attendance at school, the frequency of tuberculosis diminishes. The danger from the family is the same for the child at a later age, but through the school it is somewhat diminished. We have already considered these conditions more carefully under the influences of age. At any rate, it would be incorrect to consider cases of early tuberculosis, such as are reported by Demme, Flesch, Bosselut and Queyrat, as of congenital origin. Moreover, in some cases even the youngest children are exposed to infection from strangers.

An instructive case on this point has been reported by Wassermann: A child ten weeks old had extensive cheesy foci in the left lung, the bronchial glands, liver, kidney, and middle ear. The mother was healthy. On careful inquiry it developed that eight days after the birth of the child the mother had stayed for one week with a brother-in-law who was highly tuberculous and who expectorated indiscriminately.

Ostensible Protection through Activity of Growth.—We attempt to explain the extreme rarity of clearly demonstrated cases of congenital tuberculosis by the assumption that the increased proliferative powers of the fetal and infantile tissues hinder the development of the tubercle bacillus.

But how does this compare with the fact that in a majority of cases tuberculosis only appears many years after all growth has ceased, in one-half the cases between the ages of forty and sixty. (See statistics, page 280.)

Lately Baumgarten has declined to accept even this interpretation. According to his present conception, growth of the bacilli in the embryo and in early post-embryonal life is so much retarded that the micro-organisms are able to produce only insignificant alterations in the tissues, which escape even the most painstaking examination. After this time has elapsed (*i. e.*, in the first months, or at the very latest during the first or second year) tangible tuberculous foci develop, which the pathologist is able to detect, however, only by very careful examination. These latent foci form the starting-point of the manifestations which occur at puberty or with advanced age.

Baumgarten bases his opinion on the previously mentioned experiments of Maffucci, in which chickens from infected eggs developed macroscopic tuberculous changes only after one to four months. These results can, however, be just as well explained by the assumption that the bacilli, the greater part of which had probably died, entered the embryo just previous to its hatching, since the germinal plate itself had not been infected.

In contrast with these artificial and abnormal conditions are the numerous instances in which the progeny of tuberculous mothers remained well, even if allowed to live for long periods of time. (See page 295 seq.)

The hypothesis which attributes a heightened power of resistance to germ infection to the fetal tissues is controverted by still other facts. A glance at the mortality statistics shows that infectious diseases are more prevalent in infancy, and that the least resistance is manifested at that period of life.

Just as little can *syphilis heredetaria tarda* be adduced as proof of such powers of resistance, since it is not, indeed, in itself, sufficiently well established to afford a foundation for other hypotheses. Frequently this form of the disease is assumed in individuals with late tertiary manifestations purely because the mothers, whose history we are forced to accept, entirely overlooked the ordinary manifestations during the first few months of life (Kassowitz). However, if one desires to use syphilis, which is inadmissible for other reasons, for purposes of comparison, then it is just this disease which argues against this power of resistance, since it generally produces marked changes in the fetus, or even death of the embryo. Would any one attempt to refer a syphilis manifesting itself at thirty or forty, or even later, to the influence of heredity?

Experience, however, teaches us that tuberculosis is far more frequent during the time of the greatest growth activity, in the second to the third year (as is well known, the weight of the child is quadrupled in the first sixteen months), than it is, for example, in the sixth to tenth year, in which growth has become slower. Are not the very fetuses and newly born, in which a marked tuberculosis has been found, a proof positive that the fetal tissues are unable to offer any resistance to the tubercle bacillus after it has effected an entry?

Moreover, it is especially during infancy that tuberculosis evidences a marked tendency toward dissemination.

Weigert says that in children the tubercle virus spreads more readily than in adults; Cornil also calls attention to the marked energy with which tuberculosis of the newly born appears to spread.

Froebelius gives as his opinion that tuberculosis occurring in those of a tender age rarely ever remains localized in a few organs but becomes rapidly generalized through the aid of the lymph- and blood-vessels.

Landouzy expresses himself in a similar strain, and Michael emphasizes the fact that the tubercle virus acts with the utmost intensity if it gains access to the infant organism, in contradistinction to its action upon adults.

Henoch also claims that tuberculosis in children up to the second dentition is characterized by a violent course, and that the lethal termination is a matter of a few months or, at the most, of one or two years.

According to my previously mentioned compilation of the autopsy records from Virchow's pathological institute, comprising children up to five years of age, the tuberculous process evidences a tendency to dissemination in infancy, in the following manner:

AGE.	NUMBER OF CHILDREN.	NUMBER OF CASES IN WHICH THE FOLLOWING ORGANS SHOWED TUBERCULOUS CHANGES.															
		Lung, Pleura, and Bronchial Glands.	Larynx.	Trachea.	Pharynx.	Esophagus.	Intestine.	Mesenteric Glands.	Peritoneum.	Liver.	Spleen.	Kidney and Bladder.	Genital System.	Pericardium.	Heart.	Brain.	Bones and Joints.
0–1 year .	43	38	—	—	1	—	9	11	9	31	27	23	—	1	1	18	2
1–2 years .	83	70	2	—	3	1	10	25	19	44	43	25	1	3	1	25	13
2–3 " .	56	47	1	1	1	—	11	10	8	19	17	12	2	—	—	24	9
3–4 " .	51	41	2	1	—	—	11	19	9	24	18	15	2	1	—	23	9
4–5 " .	30	27	3	1	2	—	10	6	7	14	14	7	—	1	—	10	4
Total .	263	223	8	3	7	1	51	71	52	132	119	82	5	6	2	100	37

In view of these figures, there is no possibility of assuming an increased resistance to the tubercle bacillus during infancy, since, on the average, more than three organs were affected in each child.

The hypothesis of a greater resistance on the part of the fetal and infantile tissues is, therefore, not supported by these facts, but rather controverted.

Latency of Tuberculosis.—Since the rarity of congenital tuberculosis, as well as the comparative infrequency with which tuberculosis is disseminated among children, not only fails to support, but actually argues against, an intrauterine transmission of the germ, the attempt has been made to piece out the facts by the theory of a latent tuberculosis. According to the theory, the tubercle bacillus is transmitted *in utero,* but in the majority of cases does not proliferate. Only when certain near factors appear which weaken the organism and render the soil suitable do "the dormant horde of bacilli awake to life," then only do they proliferate, spread, and allow the disease to become evident.

This conception is based upon the fact that not infrequently in autopsies on persons dying of diseases other than tuberculosis tuberculous changes have been found which had escaped detection *intra vitam.* This tuberculosis is frequently trifling in extent or even partially or completely healed.

Lebert has already called attention to the frequency of accidental findings of tuberculosis. Baumgarten claimed that in approximately every third or fourth supposedly non-tuberculous corpse he was able to discover some latent or healed local tuberculous process. Bollinger estimates that 40 to 50 per cent. of the bodies (inclusive of those dying from tuberculosis) autopsied at the pathological institute of Munich show tuberculous changes. He says "that about one-fourth of all the adults who do not die of tuberculosis have disease of the apices." Heitler, according to the autopsy records of the pathological institute of Vienna, found cicatrized nodules in the lung in 780 (nearly 4.8 per cent.) out of 16,562 autopsies. In the autopsy record of Birch-Hirschfeld in Leipzig, tuberculosis was noted as a secondary finding in 23 to 26 per cent. of the cases; these autopsies were chiefly on adults, there being no children's hospital of any size in the city.

I may again call attention to the previously mentioned statements of Loomis, Pizzini,* Spengler, Kossel, and myself concerning glands, for the most part the bronchial glands, which were macroscopically intact, but which were proved to be tuberculous by inoculation tests, or by bacteriological or histological examination.

Since the duration of tuberculosis is, on the average, three years, and since a tuberculous individual is as susceptible to other diseases as every one else, it necessarily follows that a certain percentage of the tuberculous will die of other diseases or from accidents in the course of the three years which precede the natural termination. For this reason a number of these bodies will always show tuberculous foci in different stages of development, in the first, second, or third month, in the first, second, or third year, or, in part, either healed or in process of healing.

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* Not all of Pizzini's 12 positive inoculation experiments are free from objection. If, for example, miliary tubercles appear in the lung, liver, and spleen, within seven days after the inoculation, there is, in all probability, an error in the experiment.

The data fail to show how far the number of findings of latent tuberculosis exceeds the required proportion of cases of consumption in which the course of the disease was prematurely interrupted by an intercurrent affection; for this latter figure varies with the different periods of life, with the social standing of the deceased, in short, according to the varying dissemination of tuberculosis in each particular class of the population. The figures of pathological institutes will always be higher than those for the entire population.

These findings do not permit of a correct picture of the frequency of tuberculosis for the further reason that histological and bacteriological verifications of the tuberculous character of the cicatrices and of the other changes are largely lacking. The pathological changes might, therefore, easily be of different origin.

The number of actual findings is considerably in excess of the mathematically calculable number of cases of latent tuberculosis.

This may be due in part to the fact that all cases of healed tuberculosis are included, and that the findings have reference chiefly to glands which, especially in the child, are the most frequent seat of disease, while their recuperative power also is much greater than that of the other tissues. We have repeatedly pointed out the lymph-glands as safeguards of the body.

A correct estimate of the frequency would require an exact differentiation between actually healed cases, which can no longer be regarded as latent, those which are developing, and those which have come to a standstill but are still virulent.

The researches existing up to the present time are not sufficient, nor would they entitle us to draw far-reaching conclusions. Doubts concerning the above-mentioned interpretation must also be aroused by the circumstance that latent foci are found not only in robust individuals, but just as frequently in the feeble, in whom the bacillus must evidently have found a suitable soil.

Does the existence of these latent tuberculous foci support the doctrine of heredity? The very location, which is chiefly in the lungs and the bronchial glands, makes such an explanation appear forced, and points more naturally toward an infection by inhalation.

What biological facts entitle us to assume that the bacillus is capable of remaining latent through decades, for forty or sixty years, in the human body? Cohnheim long ago argued against the doctrine of a tubercular heredity, because he did not believe that a disease could remain latent for so long a period. Even syphilis, which is ordinarily used for purposes of comparison, fails us, since latency of such duration is entirely unknown even in this disease. A lues delayed for several years is a rare event, and yet we are asked to regard this as the general rule in consumption!

In cultures on serum, in which the bacilli are preserved for a comparatively long time, in which they encounter no antagonism, where the most favorable conditions possible exist for their preservation, they do not live more than half a year. In the human body, too, the isolated bacillus, as Koch surmised, probably speedily succumbs. At least, the demonstration of Kitasato's that most of the bacilli in the sputum are already dead speaks for this. The biology of the bacillus therefore argues against latency of such duration, and clinical observations also afford no proof of it.

If some scrofulous disease of the neck, after an apparent quiescence of years, should be followed by pulmonary tuberculosis, or if a cicatrized lupoid focus should secondarily ulcerate after the lapse of years, one might be justified in suspecting a latency for the intervening period. Logically, however, all these cases admit of the possibility of a new infection, in fact, render it extremely probable, especially if the patient has continued to live in the same or similar infectious surroundings (re-infection).

Finally, the old foci with caseous and chalky contents, such as have been successfully inoculated by Kurloff, afford no proof of a prolonged period of virulence, since their age has not been even approximately determined.

Up to the present time all proofs are lacking that the bacillus, without flourishing and proliferating, and without having been rendered harmless by encapsulation, is still capable of retaining its virulence for years and decades until offered a suitable soil. The view held by Wolff, who is inclined to find proofs of the longevity of the bacillus in the fact that he was able to stain bacilli in a focus which had evidently been silent for a long time, need hardly be refuted. On this principle bacilli which had been boiled or preserved in alcohol for decades would also have to be considered alive.

It has been suggested that spores with extreme powers of resistance may be found in these old foci. But if we hold to facts without giving free rein to the imagination, we know at present only that tuberculous material or cultures in any form, whether moist or dry, and with or without so-called spores, lose their virulence in a comparatively short time (one-half to one year), unless a suitable soil is furnished for their development.

The conception of a latent tuberculosis, therefore, affords no support to the theory of heredity.

Pathological Objections.—All doubt as to the extrauterine origin of infantile tuberculosis (to say nothing at all of the tuberculosis of adults) is entirely removed by the pathological findings. According to the law of localization (see page 105), we see the first and most advanced changes at the place where the tubercle bacilli enter the organism, that is, in the nearest lymph-glands. Accordingly, in intrauterine transmission, the liver, being the inlet for the blood infected by the maternal circulation, should show the first and most important changes. As a matter of fact, we find that in all incontestably congenital cases the liver and abdominal viscera are principally involved, whereas in the preponderating majority of tuberculous children it is not the liver, but, just as in adults, the lungs and the bronchial glands which are chiefly affected.

According to Biedert's compilation, in 1346 bodies of tuberculous children, the organs were affected in the following ratio: The lung in 79.6 per cent.; the intestine in 31.6 per cent.; the lymph-glands in 88.0 per cent.; the peritoneum in 18.3 per cent.

Leroux, in 214 autopsies of infantile phthisis, found the lung affected 211 times (no mention is made of glands); the spleen, 101 times; the liver, 82 times; the intestines, 72 times; the kidneys, 46 times; the bones, 8 times.

According to Müller, in 150 autopsies on tuberculous children, the organs were diseased as follows: The lung in 92.67 per cent.; the lymph-glands in 84.00 per cent.; the pleura in 65.30 per cent.; the spleen in 43.33 per cent.; the intestine in 38.00 per cent.; the liver in 33.30 per cent.; the kidney in 23.33 per cent.; the bones and joints in 22.00 per cent. Queyrat obtained similar results.

Flesch also designates the bronchial glands as the organs most seriously and earliest affected in the bodies of tuberculous children. According to Steiner and Neureuther, in 302 bodies of tuberculous children the lymph-glands were affected 299 times, and of these the bronchial lymph-glands 286 times.

Carr determined in 120 cases that the disease originated from the the thoracic cavity in 79 cases; from the abdomen in 20 cases; from one or the other of these cavities in 6 cases.

According to Neumann, in 47 post-mortem examinations on tuberculous children there was found tuberculosis of the bronchial glands in 10; tuberculosis of the bronchial glands and of other organs in 36; tuberculosis without participation of the bronchial glands in 1.

If bone tuberculosis occupies a prominent position in the reports of some authors,—Brandenberg, for example,—it is due mainly, as this author himself asserts, to the peculiarity of the material compiled. The same is to be said of Demme, who, however, considers that tuberculosis of the bronchial and mesenteric glands is the most frequently demonstrable disease in the cadaver.

That bone tuberculosis, as well as osteomyelitic processes, by no means points to a congenital origin has already been shown. The conspicuous frequency and extensive dissemination of pulmonary or bronchial and mesenteric tuberculosis during infancy characterize these organs as the primary foci. These facts, therefore, oppose the theory of a congenital derivation and point to an origin by inhalation or by food consumption.

Heredity and Environment.—Lastly, the extrauterine source of infantile tuberculosis is evidenced by the fact that children of tuberculous parents, in case they are removed from their family, *i. e.*, the source of the contagion, remain free from the disease.

Thus, Epstein observed in the foundling asylum at Prague that children of tuberculous mothers, nursed by healthy wet-nurses, flourished, whereas those nursed by the sick mother speedily died of tuberculosis. In four years Epstein failed to discover a case of tuberculosis in nursing infants at the foundling asylum.

In the orphan asylum at Nürnberg, with an average capacity of 100 children, many of them with a pronounced tuberculous taint, Stich saw only a single case of tuberculosis in eight years. Furthermore, he succeeded in tracing only one case among those dismissed from the institution, in spite of the fact that many were already twenty years of age.

According to Schnitzlein, in 41 per cent. of the children at the orphan asylum of Munich both parents had died of tuberculosis, and in 43 per cent. either the father or the mother. In spite of this fact he observed only two cases of tuberculosis among 620 children.

To establish these relations upon a broader basis, I sent a circular with questions on this subject to fifty-one orphan asylums. Unfortunately most of them lacked the statistics necessary for accurate answers. From the replies as far as they could be used, it was possible to determine that in a number of orphan asylums with an average annual capacity of 515, only three cases of tuberculosis were recorded within five to twenty-one years (comprising 7245 years of life). These three cases appeared only some time after their admission into the asylum, so that in spite of the marked hereditary taint of orphans the frequency of tuberculosis was diminished.

On the other hand, it must be admitted that in many other orphan asylums the average for tuberculosis is greatly in excess of this number. In view of the first group of cases, the true cause of this mortality is to be sought, not in any hereditary taint, but rather in faulty hygienic arrangements and in the crowded condition of the inmates, which increases the opportunities for infection when the disease is once introduced.

If the children, after their discharge from the orphan asylum, are exposed to numerous sources of infection in their workshops, they succumb as speedily as do those without any hereditary taint.

We are indebted to Bernheim for an interesting contribution to these questions. He found that the progeny of tuberculous rabbits, guinea-pigs, and dogs became tuberculous if they remained with their parents, but, on the contrary, remained well if they were instantly removed after birth. The previously mentioned author had the opportunity of delivering three tuberculous women of twins. He insisted each time that one child should be nursed by a healthy wet-nurse living together with the mother, the other child being sent to the country. In all three cases the children at home died, whereas those sent to the country remained well.

Deductions.—If we sum up what we know about the hereditary transmission of the tubercle bacillus, we find:

1. The assumption of a seminal transmission of the tubercle bacillus (a hereditary transmission from the paternal side) lacks all foundation.

2. The placental transmission is, however, undoubtedly possible. But up to the present time the extremely small number of recorded cases, in spite of the fact that for many years the attention of numerous pathologists has been constantly directed to this point, together with the results of animal experiments, as well as clinical, pathological, and statistical data, make it appear that such transmission is extremely rare, and dependent on special conditions, such as advanced uterine tuberculosis with placental hemorrhages.

On the whole, one would do well in each case, unless time and circumstances correspond to the previously mentioned conditions, to be as skeptical toward the assumption of a hereditary transmission as one should be toward "idiopathic" and "rheumatic" suppurations; conceptions which formerly circulated so freely, but which in the light of modern research have dwindled to a very questionable existence.

A real practical significance is not to be attributed to such transmission, all the more since such fetuses and children seem to die speedily.

[The doctrine of the latency of tuberculosis has very recently received a strong impulse from an address by Professor Behring,* in which he maintains that most pulmonary phthisis is the result of an infection acquired in infancy from food, and which has remained latent in the mean time; that "the main source to which phthisis must be traced is the milk diet of suckling infants." This conclusion is based partly upon the demonstrated fact that the digestive system of new-born mammals lacks the protective mechanism against infection which is characteristic of it in later life.

However, this conclusion will not appeal to the majority of clinicians. The arguments which Cornet brings forward against the latency of infantile tuberculosis hold good also in the present instance. The weight of clinical observation, moreover, is strongly against this view, pointing as it does convincingly to the usual transmission of the disease from one person to another. The tendency for cases to follow one another in certain families, and the existence of foci of infection in the thickly settled portions of most large cities, all point in the same direction, while the results of animal experimentation prove beyond question the ready possibility of conveying the disease by the inhalation of either dried or moist sputum, or other material containing virulent bacilli.

At the present time, when the public has reached an understanding of the danger of infection from consumptives, when legislation in many countries has been introduced to control this danger, and when we have seen following this a marked improvement in tuberculosis statistics, it is wiser that nothing should be done to shake the confidence of the public in these precautions except upon the ground of absolute proof. Pending the settlement of these difficult questions, it is best that strict precautions should be taken against infection, both from other consumptives and from the milk of tuberculous cattle.—Ed.]

ATAVISM.

If the direct transmission from mother to child is only a rare exception, the assumption of an atavistic transmission from the grandparents, passing over the healthy parents (as is urged by some ardent disciples of the theory of heredity), hardly requires serious refutation.

Granted that properties and singularities of the organism are transmitted by atavism, the transmission of a living vegetable parasite does not even remotely admit of a comparison. Even in syphilis, the hereditary disease κατ' ἐξοχήν, no one attempts to maintain an atavistic transmission. One would have to suppose that the tubercle bacillus passed from grandparents either to the father or the mother, which is contrary to all laws of localization, and that it settled in the ovary or testicle, where it lived for years without multiplying. Then, since there can here be question only of isolated germs, just at the moment of cohabitation it "straddled" that particular sperm cell which out of the many thousands* ejaculated was intended for fecundation, and entered the ovum. Let him who can conceive this! With a scientific trend of mind such a course of reasoning is impossible.

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* Deut. med. Woch., Sept., 1903.

HEREDITARY DISPOSITION.

I mentioned in the introduction to this chapter that some physicians, and indeed a vast majority of them, understand by hereditary tuberculosis only the transmission of a certain predisposition. Numerous data exist which are intended to prove this form of heredity.

REPUTED FREQUENCY.

In the following order of frequency phthisis is looked upon by these authors as hereditary:

Louis	in	10	per cent.
Hirschsprung		10	"
Barthez and Rilliet	about	14	"
Lebert	"	17	"
Pidoux, Piorry, Walsche	"	25	"
Schäffer (310 consumptives)	"	26	"
Jacubasch.		27	"
Briquet	about	33	"
Cotton	"	33	"
Herard, Cornil and Hanot (100 consumptives)	"	38	"
Bockendahl	"	47	"
Hill	"	50	"
Leudet	more than	50	"
Demme	" "	50	"
Valin		50	"
Solly (250 consumptives)	about	55	"
Of these through the parents		29	"
" " " " grandparents		7	"
" " " " relatives		19	"

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* Lode reckons about 226,000,000 spermatozoa to one seminal emission in man.

Fuller	60	per cent.
Of these through the parents	26	"
" " " " grandparents	17	"
" " " " uncles and aunts	15	"
Portal	about 67	"
Haupt (1088 consumptives)	67	"
Mayet	70	"
Rufz	about 85	"

The marked discrepancy in the percentages (10 to 85 per cent.) of the different authors is from the very outset an indication that the conception of heredity is extremely elastic, and that the figures are determined not by objective facts, but by the subjective opinion of the observer.

Whereas some describe a hereditary taint only if the mother or either of the parents is affected with tuberculosis, others take the grandparents into consideration; while others, again, consider the brothers and sisters of the parents (so called collateral heredity). Even these are exceeded by those who construe a tuberculosis of any relation, whether in an ascending or collateral branch, as a hereditary factor.

These figures merely serve to show approximately how often more than one case of tuberculosis occurs in a family. In no way, however, are the statistics at present available such as to satisfy the demands of a rigid critic.

DEFECTS OF THE AVAILABLE STATISTICS.

In the first place, the figures on which the percentages are based are frequently much too small. Statistics (which fact is again and again overlooked in medicine) is the law of great figures. It is only by these that fluctuations and chance occurrences, the natural sources of error which occasion noticeable difference in small figures, are neutralized. The apologetic assurance of some authors, that "the small material was selected with especial care," shows little appreciation of the theory of statistics and of what is to be required and derived from them. Small figures are of no value at all in statistics. If this were only kept in mind the continual contradictions in medical statistics would, in part at least, be avoided.

In the second place, deductions as to hereditary influences based on these figures are built on a structure of logical errors and omissions.

The mere fact that with a certain proportion of patients the same disease has previously appeared in the family does not prove a causal relationship. In scarlet fever also, for example, we find that the parents have likewise had scarlet fever, yet no one thinks of a hereditary transmission. This idea can only be entertained if it is proved that a disease occurs exclusively, or at least with marked frequency, in the descendants of people affected with the same disease, as compared with other individuals.

If we figure up the relatives of a consumptive, we have:

The parents of the patient	2 persons
The grandparents on both sides	4 "
On the average, two brothers and sisters of each of the parents	4 "
Brothers and sisters of the patient	2 "
	12 persons

If, following certain authors,—*e. g.*, Wolff,—we add to this the cousins, we have in all a total of sixteen to twenty persons. The mortality statistics show that, on the average, out of 7 deaths at any age, 1 is due to consumption; out of 6 deaths over age of one, 1 is due to consumption; out of 2.5 deaths between twenty and sixty, 1 is due to consumption. In view of these facts, it is certainly not astonishing if among those who have died in the family of a consumptive there are one to two deaths from tuberculosis. On the contrary, this corresponds exactly to the average percentages for the entire population.

To deduce a hereditary influence from these facts is, therefore, a conclusion mathematically incorrect. At the very least, it would have to be demonstrated numerically that in the families of non-tuberculous persons tuberculosis did not occur with even approximately the same frequency as in the families of consumptives. In no statistics hitherto compiled has any attempt been made to demonstrate this fact; much less have any succeeded in proving it.

Kuthri (quoted from Dürck) tested the question of the comparative frequency of tuberculosis in the parents of tuberculous and non-tuberculous patients. He was unable to find any important difference in spite of careful anamnestic inquiries. Thus he found among 432 consumptives: Father tuberculous in 10.5 per cent.; mother tuberculous in 9 per cent.; both parents tuberculous in 2.4 per cent. Among 108 non-tuberculous patients: Father tuberculous in 9.2 per cent.; mother tuberculous in 9.2 per cent.; both parents tuberculous in 1.0 per cent.

Even by demonstrating that the children of consumptives more frequently succumb to this disease than do those of healthy parents, the advocates of this theory would not have proved a hereditary transmission.

The greater frequency could just as well be caused by the increased opportunities for infection afforded by intimate intercourse with tuberculous parents or relatives. Most authors commit the error of arbitrarily selecting heredity from these two possibilities and entirely ignoring the other.

Logically, therefore, a hereditary influence could be positively assumed only when the individual in question had been removed from the circle of the family and relatives and an increased opportunity for infection through the family or other conditions could be excluded. No statistics hitherto collected satisfy these requirements.* On the contrary, most authors simply content themselves with discovering a tuberculosis in some more or less distant relation, from which they fallaciously argue a "hereditary taint."

Such compilations, therefore, do not constitute scientific statistics. They afford a distorted picture, and cannot serve as a foundation for the doctrine of heredity.

One frequently hears the assertion that every experienced physician can cite numerous instances in which the children of consumptives, even if separated from their parents, successively become tuberculous, often just at a certain age. Aside from the questionable value of such rhetorical hyperboles ("every physician—numerous," unless verified by a number of examples), the few cases reported in the literature on the subject afford very inadequate proofs; for evidence is lacking that the children in question were not already tuberculous at the time of their separation, or that further opportunities for infection were excluded.

All these researches, even if restricted to the parents of the patient, suffer from a defect, previously mentioned, which renders them from the outset useless in determining this question. As a rule, they are all based on the fact that either of the parents was tuberculous, without any regard for the time at which the disease developed. They embrace cases entirely irrelevant as regards heredity; cases in which the parents were still in good health at the time of conception and pregnancy, and became diseased only ten to twenty years subsequent to those events, at a period when the child had already become infected with the disease or perhaps died of it. In connection with such data, the "previous question" often presents itself as to how often the parents became "tainted" or infected through the children.

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* Brandenberg, in a thesis done under Hagenbach-Burkhardt, very correctly maintains that these data simply indicate the chances of infection within the family of the patient.

How necessary it is to regard this relation in time is evident from my previously mentioned researches. Thus, in 751 families there died of tuberculosis, subsequent to the birth of the child which had first acquired the disease, in the first quinquennium, 14 fathers and 16 mothers; in the second quinquennium, 23 fathers and 19 mothers. If the suspected cases (three fathers and three mothers) be added to these, the total for the first ten years after the birth amounts to 40 fathers and 38 mothers; whereas, after the tenth year, if we include the suspected cases (20 fathers and 22 mothers)—125 fathers and 139 mothers, in all, died of tuberculosis. In these cases, at the time of the labor in question, tuberculosis was practically excluded.

The further deductions, which are to a great extent derived from the figures already cited, can only be ascribed to an absolutely preconceived belief in heredity. As examples, we may adduce the following: That a hereditary tuberculosis develops at a less advanced age than the acquired (Leudet); that it generally develops in infancy or youth, whereas the acquired is manifested fairly late in life (Hanot); that considerably more than one-half the victims of inherited consumption are carried off before thirty, and that after the fiftieth year of life hardly one-tenth are still living (Bockendahl).

The facts which are at the basis of these assertions are readily understood from the point of view of family infection. The circle of persons with whom children associate is chiefly restricted to the family; even during their school-years the association with other children is unimportant as regards the danger of infection. A glance at the statistics teaches us that tuberculosis is less frequent among school-children, *i. e.*, in the corresponding age, than it is in later years.

If children become tuberculous, the source of the infection is, as a rule, to be found in the family. The fact is thus explained that in the early years of life heredity appears to play an important rôle, and that pediatrists are especially apt to misconstrue the facts.

With adults, on the contrary, who for the most part have long been separated from their families, or who, on account of their occupation, come in contact with strangers during the day, the disease is accordingly frequently traceable to an infection from strangers, and the figures for heredity remain low.

The apparent predominance of inheritance through the mother or grandmother, as opposed to the father, which various authors emphasize (Leudet), finds its natural explanation from the standpoint of infection in the fact that the female members of the family stay at home much more than the men do, and that the care and education of the children are chiefly in their hands.

One is surprised on careful, critical examination to find on how few exact facts the doctrine of heredity in tuberculosis is based.*

This is not the place for detailed criticism. If I make an exception of Riffel's treatise, I am justified by the circumstance that his work is frequently quoted as the main support of the doctrine of heredity. Riffel has decorated 112 pages with about 100 gross errors of fact and contradictions. The remarkable longevity of some patients I will not even consider. One man, who married in 1781, marries again more than one hundred years later.

The dead also, whom Riffel frequently has dying at different ages, I would permit to rest in peace, and not marry them again decades after their death, as Riffel does. Women are changed to men; one girl marries at eight; a boy dies at one year of age, but marries, neverthelesss, eighteen and twenty years later; a girl dies one month, and marries a widower thirty years later, giving birth to seven children; a relative of Riffel's is born twenty-four years after her marriage! He seems to have as little success with the multiplication table as (according to his own admission) with cultures of the tubercle bacillus; for he counts from the year 1883 to the year 1886 as sixteen days, from 1885 to 1888 as one month, from 1797 to 1799 as ten months, from 1831 to 1876, once as forty-four, and again as forty-seven years, etc. In short, the entire dissertation teems with mistakes; nevertheless Haupt calls the work "thorough and competent"; F. Wolff, "valuable." There is nothing more excellent than modest demands! I know of no more faulty and less scientific work in all medical literature. And this is to furnish the "positive proof" of heredity!

Our so-called experience is of as little use in deciding this question as are the statistics which are at present available. For into what errors experience can lead, unless it can be put into figures, is shown by the ancient axiom that the prime of life furnishes most victims to tuberculosis. Yet it is to-day an incontestable fact that this assumption—even if it does still appear in certain text-books—is absolutely false (see page 281).

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* With how little care such researches are conducted is illustrated by the following example. In a work very frequently quoted in support of the doctrine of heredity, I found that a small table, occupying hardly one-third of a page, contained nine mistakes in figures, or misprints, on which the author, who particularly emphasizes the exactness of his observations, bases his conclusions.

OTHER GROUNDS OF HEREDITARY PREDISPOSITION.

It is a question whether such an assumption is not justifiable up to a certain point, for intrinsic reasons. It cannot be doubted that certain qualities of the parents are transmitted to the children; thus, the color of the hair, the eyes, the stature, as well as strength and weakness.

We can understand, therefore, that children whose parents, and especially the mother, were weakened by tuberculosis, or cancer, or typhoid, or any other disease, at the time of conception or parturition, are born weaker and are more susceptible to infection than the children of healthy parents.*

We know that in a tuberculosis depending on the virulence of the infection a more or less marked poisoning of the organism with bacterial proteins occurs, which sooner or later leads to the death of the individual. It is possible that these bacterial poisons held in solution by the blood are able, under certain conditions, to affect the composition of the seminal fluid; and it is *à priori* probable that they are able to pass by endosmosis from the maternal circulation through the placenta to the fetus.

Even if clinical and experimental facts show the placenta to be impervious to corpuscular elements and bacteria, and reveal it as a barrier broken through only in the rarest cases and under abnormal conditions, as through lesions of vessels or other pathological changes, nevertheless it is an entirely different matter when the question is one of chemical bodies which are soluble and diffusible. The researches of Schauenstein and Späth (1858), Mayer (1877), and especially of Gusserow and others, have proved that, in contrast to solid bodies, soluble substances such as potassium ferrocyanid, potassium iodid, or sodium salicylate pass in part from the maternal blood to the fetus. It is possible, therefore, to assume a partial transmission of the tubercle proteids, the assimilation of which by the blood is marked by constitutional symptoms, such as loss in weight, anemia, fever, etc. This may be supposed to occur, especially in advanced tuberculosis of the mother, whose blood is practically supersaturated with these poisons.

For the most part, such children die *in utero* and give rise to miscarriage, an event which, according to clinical and veterinary experience (Siegen), is not at all uncommon in consumptive mothers; or they die soon after birth, under the clinical picture of marasmus and atrophy, without any recognizable cause.

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* In my dissertation on this point which appeared in 1888 I expressed myself almost in these words, a fact which I desire to emphasize particularly for the benefit of those authors (Bollinger and others) who credited me with an absolute denial of predisposition.

In milder degrees of poisoning of this kind, and with the most painstaking care, it is possible to keep such children alive for a longer time, perhaps even indefinitely. The transuded toxins are gradually eliminated from the body, either before or after they have left permanent and irreparable traces upon the development of the organism.

From experiments on animals (which experiments, it is true, do not exist in great number) it appears that an organism which is already under the influence of the tubercle proteins possesses a certain hypersensitiveness for the tubercle virus, and when a new infection or intoxication occurs (such as is produced by incorporating even the weakest doses of living or dead bacilli) it succumbs with remarkable rapidity. Possibly this may find a similar application in man. For the present these are only theories, although on the basis of such experimental results their plausibility cannot be gainsaid.

The influence exerted upon the fetus very likely depends on the extent to which the disease has advanced in the mother at the time of pregnancy. A similar influence, though in a less degree, may possibly be exerted by the father. But all these points still require a more thorough clinical and experimental study. One must first learn to omit the customary inference of a "hereditary taint" in the histories of patients, whenever any more or less distant member of the family becomes consumptive, no matter what the place or when the time; one must first impose upon himself the wise restriction of selecting only cases in which the father and mother were really tuberculous at the time in question, and then pursue the further history of these cases. Only then will it be possible to obtain credible and perhaps valuable information on these points. The influence of a "hereditary taint" will then appear of more modest dimensions, and will at the same time be more clearly defined. As it is, all the information which we at present possess is valueless in solving the problem of hereditary tuberculosis.

In any event, a decisive rôle in determining the march and distribution of the scourge can never be attributed to hereditary predisposition. This is a conclusion concerning which prophylactics and therapeutics may well take heed.

CHAPTER VII.

PREDISPOSITION.

Aside from a possible specific susceptibility for the tubercle virus, inherited from tuberculous parents and especially from tuberculous mothers, it is generally assumed that a certain weakness, a somatic inferiority, belongs to the children of parents who are sick from any cause, or are weak or aged, and, according to Brehmer, especially to the children of mothers who have had rapidly recurring pregnancies. This weakness renders such children more liable to infection by the tubercle bacillus (hereditary predisposition); the condition may also be acquired during extrauterine life, either during the period of growth or later (acquired predisposition). The habitus phthisicus, characterized by a narrow chest, with long vertical diameter and long thin neck, is the most expressive sign of such hereditary predisposition.

Predisposition Frequently Equivalent to Exposure.—The theory of predisposition is old. It emanated from the conception of consumption as a peculiarity of constitution, and is, at the same time, a corollary of the doctrine of dyscrasiæ, and forms the connecting-link between the latter and the tubercle bacillus. Formerly the assumption of predisposition was considered necessary to explain the immunity of many people against the supposedly universal dissemination of the tubercle bacillus. But since the doctrine of ubiquity has shown itself to be unfounded, and since we know that tubercle bacilli exist in considerable number or in virulent condition only in the dwellings of consumptives, and, furthermore, since we have found, in the foregoing chapter on Infection, that the danger of infection is really very unequal for different people, though apparently living under the same conditions, it becomes necessary carefully to estimate all the conditions of environment which bear upon the exposure of the individual before we can ascribe the presence or absence of an infection to causes lying within that individual himself.

Degree of Danger.—There are certain contagious diseases in which the susceptibility of the individual appears to play an important rôle. Tuberculosis, on the other hand, appears to belong to the same type of disease as smallpox and syphilis, to which all, or nearly all, people are susceptible. The fact that different species show a varying degree of resistance to the development of the tubercle bacillus (*e. g.*, dogs are more resistant than guinea-pigs) does not entitle us to assume that individuals of one and the same species, "man" likewise, exhibit a difference in resistance amounting in some to an absolute immunity.

For that reason the susceptible cannot be contrasted with the immune, since the difference is one of degree, and a marked lack of susceptibility may be overcome by an increased exposure to infection or infectious material. The fact that one-seventh of all persons die of tuberculosis, and that tuberculous foci are found in numerous other bodies in addition, ought to be a sufficient warning against granting a decisive practical importance to this so-called relative immunity.

In many cases the quantitative and qualitative degree of exposure to infection affords us an explanation which formerly could be explained only by an increased or diminished susceptibility. The notion that predisposition is as important for the occurrence of a disease as infection, or even more so than the bacillus, must be repudiated as unsupported by the evidence. We frequently find that the healthiest and strongest individuals, who show no hereditary taint and who have not been weakened by excesses or previous diseases, easily fall victims to consumption and readily succumb to the disease. It is only necessary to recall the tuberculosis of champion wrestlers and that of prize cattle.

Nature of Predisposition.—If one defines predisposition in the customary manner, as "a specific vulnerability," "a weakness of the vital processes," as "a general depression," as "a disproportion between the capacity of the organism for work and the work which it must perform," little is gained, since by these phrases we do not express an exact idea, but merely circumscribe what we do not know. "La prédisposition est un mot pour masquer notre ignorance," says the clinician G. Sée.

I will not attempt to deny that there are a number of factors which may increase the susceptibility of an individual to a considerable degree, and which have a very decided influence on the course of the disease when an infection has taken place.

Predisposition may be understood as determined either by the body-fluids (chemical or humoral) or by the vital energy of the cell (cellular); but since the one is dependent on the other, no sharp differentiation is possible. Furthermore, predisposition may be general or restricted to certain organs. Lastly, it may be due entirely to mechanical conditions.

Concerning the so-called natural humoral disposition we have practically no data. It is true that in a number of other infectious diseases one person is more susceptible than another; certain ones remain unaffected, though living in the midst of people suffering from the disease. Nevertheless it remains an open question whether the exposure to infection is not more apparent than real, as we found (in the chapter on Infection) in other cases, and whether the germs really come into contact with a site which permits their development. The occurrence of pneumococci in the mouth is not positive evidence, since the mouth offers as unfavorable a soil for the development of the pneumococcus and the streptococcus as does the skin itself. Even in those who show a marked predisposition for pneumonia we do not find any proliferation of the pneumococcus in the mouth, and we are justified in concluding that a proliferation of pneumococci (under the picture of a pneumonia) occurs only when the aveoli or terminal air-passages have been invaded. We might, perhaps, more justly regard the presence of cholera vibrios in the intestine during health as constituting a predisposition to the disease. But how far the presence of certain other bacteria determines the clinical picture of cholera, still remains a disputed point. The demonstration that pathogenic germs can exist during health as harmless parasites in localities really suited to their development is as yet by no means perfect, the more so since morphological similarity and even apparent pathogenity do not prove identity, as we have only recently learned from the similarity between the tubercle and the butter bacillus.

The fact that people who have recovered from certain infectious diseases remain immune to them for some time may justly be cited in favor of a humoral predisposition, and on this Behring successfully founded his invaluable discovery of diphtheria serum. But this immunity is only temporary, and its duration is entirely variable for the different infectious diseases. In some it is practically absent. Again, in other diseases—for example, erysipelas, malaria, pneumonia, influenza, and articular rheumatism—it seems that one attack predisposes the body to subsequent attacks of the same disease.

In tuberculosis we cannot say from experience that any one who has successfully withstood the disease once, and in whom a tuberculous focus has healed, is protected from reinfection for a longer or shorter period of time. Indeed, it almost appears as if tuberculosis belonged to the latter category, for only too frequently we find that the cure of a case of scrofula with caseous glands is followed within a few years by an apical catarrh, a lupus, or a joint focus; that a new infection takes place which frequently proceeds without interruption to a fatal termination.

The following facts raise further doubts: One frequently observes in the same individual that in one organ the tuberculosis has healed, while it progresses in another, nay, even at the same time and in the same organ (*e. g.*, in the lung or in the intestines) one focus heals and another increases in size. One even finds that the same focus, *e. g.*, a cavity, shows extensive areas of cicatrization, and directly next to them or in between a tendency to rapid disorganization. How, then, can we explain predisposition on the basis of the body-fluids, which, surely, ought to be the same within the confines of a single organ? Might we not expect that the entire organism, or at least an entire organ, should show the same tendency, either for healing or for destruction?

Since the theory of natural immunity against tuberculosis as a property of the body-fluids is practically based on suppositions, it is not necessary to discuss the various theories, and the incomplete experiments, of Koch, Grancher and Martin, Lannelongue (negative), Klebs, Foa, Ogata and Jasuharah, Héricourt and Richet, Babes, Kitasato, Maragliano, and Behring. Moreover, not even the artificial production of immunity would furnish proof of its existence as a natural property.

The supposition that similar cells possess varying powers of resistance (whether it be on the basis of Metschnikoff's phagocytosis theory, or from any other point of view) is for the present not so well established that it can be taken into account as a factor of any weight.

It is certain that the difference in the susceptibility of different organs is due to the variable resistance which the different cells oppose to the entrance of the bacilli. Thus, it is undoubted that the skin, with its cornified epithelium, is less predisposed to, or, more correctly speaking, better protected against, the invasion of bacilli than the mucous membrane; that, furthermore, the epithelium of the mucous membrane affords a greater protection than the endothelial lining of vessels. We have learned to recognize the protection which thick squamous epithelium, especially that of the esophagus and vagina, affords. Uninjured ciliated epithelium, especially that of the respiratory organs, also affords great protection against bacteria, since it drives out those which settle in the trachea and the bronchi, even to their ultimate ramifications. Its strength and its capacity for work vary. Just as catarrhal conditions (see page 176) can weaken it, and render infection easier, so all weakening diseases, anemias, convalescence, acute or chronic alcohol poisoning (in the stage of paralysis), advanced age, impaired innervation or descent from weakened parents, produce marked variations in the energy and strength of the epithelium; so that in one individual the inspired bacilli are again carried out, whereas in another the cell energy appears to be unequal to the task. Unfortunately, only a few investigations have been made upon this point.

The parts of the lung which have become immobilized by old pleuritic process are, as one may readily suppose, more exposed to infection, on account of the increased difficulty attending the removal of bacilli. Similarly, all diseases which either partially or completely obstruct the nasal passages and necessitate mouth-breathing, thus shortening the length of the respiratory tract and eliminating two important filters, facilitate infection.

Formerly the susceptibility of the different organs was estimated according to the frequency with which tuberculosis was found in them. By experiments on animals it has been shown that these figures merely indicate the degree of their accessibility to the inroads of the bacillus. Thus, the lungs appear to have the most marked predisposition, because the bacilli have most frequent opportunity to enter the tissues of the body by way of the respiratory tract (see page 179); again, in miliary tuberculosis the lungs are the first filter through which the bacilli, having found their way into the venous circulation, are compelled to pass. That a marked susceptibility of the lungs really exists is extremely doubtful.

The udder of the cow is more frequently affected than the mammary gland in women, which indicates, apparently, a greater susceptibility of the former organ. The true explanation, however, is this, that the habit of moistening the hands with saliva in milking is very general, and that tuberculous milkmaids especially, by hawking to increase the flow of saliva, very readily convey bacilli through their sputum to the udder. In human beings the mammary gland is handled but little, but here also its occurrence, especially in sexually mature women, gives us a hint as to its origin.

The apparent predisposition of the lymph-glands, the intestine, the larynx, and other organs of the body depends largely, as was explained in the paragraphs upon infection, and can frequently be explained, on purely mechanical principles. The separate points are fully discussed under their various headings (see pages 111, 116, 120, 124, 126, 130, 134, 144, 152, 154, 157, 161, 169, 180, etc.).

There are still a number of other factors which must be taken into account as predisposing to tuberculosis, namely:

Age and Sex.—The reaction of the individual to the tubercle bacillus varies according to age. The frequency, indeed, with which the disease is found at different ages does not depend upon individual peculiarities, but is determined by entirely extraneous causes, and must be explained by the degree of exposure to which each period of life is subject (see page 279 seq.). The different results which the tubercle bacillus produces when it has once become localized must, however, have their causes in the organism itself.

In children diseases of the lymph-glands predominate; in adults, localization is in the mucous membranes and the respective organs which are invested with those membranes. The child, after the inhalation of bacilli, develops swollen and cheesy bronchial glands; the lung is frequently not at all affected, or only secondarily from the lymph-glands, as the location of the foci at the hilus, and not at the apex of the lung, demonstrates. In adults, on the other hand, the alveoli and terminal air-passages are the starting-points of the disease, and the lymph-glands are only secondarily affected.

In the child the mesenteric glands are prone to become affected, the intestines are frequently normal; in adults, on the contrary, extensive ulcerations occupy the intestinal mucous membranes, while tuberculosis of the mesenteric glands is insignificant.

Since it has been proved by several hundred experiments on young animals that bacilli can pass through healthy mucous membranes, there can be no doubt that the tuberculosis of the bronchial and mesenteric glands in children is due to the entrance of bacilli through the normal respiratory and intestinal mucous membranes. The mucous membranes of children are less impassable, the lymph-channels, as is generally accepted (Hüter), are broader or, at any rate, more pervious to the bacilli, so that they progress uninterruptedly, and meet their first check at the lymph-glands. Similarly, tuberculosis of the cervical lymphatic glands is to be traced to the entrance of bacilli through the mucous membranes of the nose, the oropharynx and nasopharynx, the tonsils, the conjunctiva, etc.

In the adult, in whom the lymph-channels are more impassable and clogged in places like an old filter,—I need only mention the numerous particles of carbon which in old lungs can be seen to clog the channels,—the bacillus is arrested earlier and proliferates closer to the point of entry. The skin shows similar differences; the fine, tender skin of a child is less impassable than it becomes in later years.

The degree in which these tissues are pervious varies in the following order: First come the mucous membranes of children. The bacillus passes through, and is arrested by the cervical, bronchial, or mesenteric lymph-glands. The mucous membranes of adults are less passable: the bacillus is stopped either in the mucous membrane or directly under it, and only after it has spread out over a fairly large area does it find some open channel to the lymph-glands.

Then the skin of children barely permits the bacillus to enter, hence the relative frequency of lupus in youth, sometimes with participation of the glands, sometimes without. Lastly, the skin of adults, if attacked, opposes the invasion of the bacilli with an almost impenetrable barrier of epithelium and connective tissue. For this reason lupus occurs much more rarely at this age, and if there is an actual injury present (*e. g.*, in autopsies or in tuberculosis verrucosa cutis), the focus tends to remain localized and the glands become affected rarely, and only then with extensive foci or deep wounds.

Sex also is of importance. The female skin is intermediate in texture between the skin of the adult man and that of a child. We find lupus less frequently in women than in children, but more frequently than in men, while, conversely, the local tubercular affections of the oropharynx occur in women more frequently than in children, but less frequently than in men.

F. Block found that of 144 cases of lupus, 46, or 31.9 per cent., were males, 68.1 per cent. were females. More than half the cases began in the first decade. According to Sachs, among 161 cases of lupus, 37.88 per cent. were males and 62.11 per cent. females. Here also the disease generally makes its appearance before the twenty-fifth year.

Of 138 cases of tuberculous diseases of the mouth and nose, exclusive of adenoid vegetations, which I have collected from literature, there were:

0 to 9 years of age, male	0; female	2
10 to 19 " " " "	4; "	5
Over 20 " " " "	108; "	19
	112	26

These affections are, therefore, extremely rare in youth, and occur much more frequently in men than in women. The extreme rarity of laryngeal tuberculosis in infancy can be explained on the same grounds.

Furthermore, in youth the bacilli escape from the lymph-glands, which are fairly reliable as filters, more readily than in adults, spread through the lymph-channels, enter the circulation, owing to the vulnerability of the blood-vessels in infancy, and readily produce a miliary tuberculosis, a disease which plays a far more important part in children and young animals than it does in later years. The variations in the course of pulmonary tuberculosis at different ages which are produced by these factors will be discussed further on.

Pregnancy.—That pregnancy has an influence on the development of pulmonary tuberculosis has not been ascertained (its influence on the course will be discussed later on), but the occurrence of a renal tuberculosis has been attributed to it, and, similarly, a tuberculosis of the mammary glands during lactation.

Climate.—Formerly, a certain degree of freedom from tuberculosis was attributed to warm climates, and patients were sent to such places to recover their health. Other authors (Pogacnik and others) maintain that heat favors the development of tuberculosis more than cold. At a later period, high altitudes were considered to be free from tuberculosis. Some consider the chief requisite to be an equable temperature with slight variations, and emphasize the bad effects of colds; Hirsch, on the other hand, has established the fact that consumption is a rare disease in the uneven temperatures of the Kirghiz-Steppe and the mountains of Germany. According to Grimshaw, marshy regions are not deleterious to consumptives, but rather the reverse, and Lievin reports that the mortality of Danzig was higher after the making of canals than before; other authors report similarly upon other places; whereas Bowditch considers a moist soil as of great importance for the development of tuberculosis, and v. Ziemssen refers the decrease of tuberculosis in Munich to the sanitation of the city. In general, a dry climate is considered as rather favorable; on the other hand, Weber found a low mortality from consumption in the humid climates of Denmark and Holland, and ocean voyages are recommended both prophylactically and therapeutically. From these contradictory statements we see that there is hardly a climate which has not been at one time looked upon as predisposing to the disease; at another, as curing it.

This much is certain, that consumption occurs in all localities, at all altitudes, with this qualification, that the more isolated and less densely populated a place, the less is the possibility of infection.

The true nature of the apparent immunity is explained by the rapid spread of tuberculosis in certain valleys of the French Alps after cases had been introduced into localities where formerly the disease had been unknown. That high altitudes have a certain influence I would not deny absolutely, since particles of dust fall more easily in rarefied air, which naturally diminishes the danger of infection and renders a subsequent mixed infection less likely to occur. This fact is also signalized by the small number of germs found in mountain air (Miquel).

How unimportant is the influence of cold or wet or change of temperature has already been shown (see page 282) by the statistics concerning miners, who, in spite of their unhygienic surroundings, show only a small percentage of consumptives. Monkeys are often cited in proof of the deleterious influence of change of climate, especially when associated with imprisonment. It is said that after they have been imported to us from their warmer climate, they invariably die of tuberculosis within a short time. This reasoning is narrow. Might not the infection be due as well to tuberculous companions in confinement (monkey's cough), to keepers, or to visitors?

Kraus, in Schönbrunn, who is versed in this subject, actually expresses it as his opinion that monkeys are infected in the cages of the dealers, since in his experience they remain well if imported directly and not exposed to infection, notwithstanding the change of climate, the confinement, and their depression of spirits.

Social Conditions.—Unhealthy social conditions, inadequate dwellings, sedentary habits, have for ages been held as predisposing to tuberculosis and to scrofula. We know from experience that tuberculosis is frequent among individuals living under such harmful conditions. "Sociale misère" is, however, inseparable from overcrowding in dwellings, and this, as well as the indoor confinement, offers an increased opportunity for infection, which is considerably enhanced by the lack of light and air in the dwellings of the lower classes (see pages 46, 84, 266, 270). As long as the latter factor cannot be excluded it is impossible to obtain a correct idea of the importance of an increased hereditary susceptibility. Poor food and poor blood are considered of especially great importance.

According to De Toma, only animals confined in the dark and insufficiently fed became tuberculous by inhalation; according to Preuss, they became infected more easily as a result of fasting and diabetes. In my experiments, and those of others, they were infected without exception, even with the best possible nourishment, when exposed to virulent infectious material.

Formerly, when the diagnosis was made only late in the disease after the characteristic anemia had appeared, the difference between the healthy and the sickly consumptives was still more pronounced. Impressions from practice appear to confirm the fact that improperly and insufficiently nourished individuals are more frequently affected with consumption than those who are well nourished. Unfortunately, there are no reliable data which take into account the possible exposure to infection, and one is inclined to doubt the correctness of these impressions when, as so frequently happens, he meets consumptives who are strong and extremely well nourished. The general condition is of much greater importance for the course than for the origin of the disease.

By way of emphasizing the fact that social conditions, faulty nutrition, and want should not be overestimated, I may adduce the observations of Virchow, who while studying typhus fever in Oberschlesien (1848) was surprised to find tuberculosis remarkably rare among the inhabitants. The professional faster Cetti was tuberculous, according to Klemperer; according to Senator, he had a cicatricial infiltration of the apex; nevertheless, it is not known that his repeated periods of fasting ever entailed any exacerbation of the disease.

The theory of M. Bidder, according to which predisposition to tuberculosis depends partly on the quantitative relation between the potassium and the sodium salts (based on the richness in potassium, and the deficiency in sodium salts, of the ashes and food of the "predisposed" herbivorous animals) has been tested by E. Israel on animals (rabbits and rats) by feeding, with entirely negative results.

Another author considers acids as predisposing factors because he knew a vigorous and healthy woman with a great relish for salad who died of tuberculosis!

Overexertion; Cares.—Bodily and mental overexertions, emotional excitements, overpowering cares and sorrows, as well as excesses and a fast, pleasure-seeking life, are all considered predisposing factors. That they have a certain influence on the origin, but especially on the course (*vide infra*) of the disease, cannot be denied, since they directly diminish the vegetative functions, and also impair the nutrition of the entire organism.

For a long time it has been believed that the widespread occurrence of **tuberculosis in the army** is due to the influence of predisposing factors. A few years ago Schmidt, of Bollinger's school, compared the military and civil population from this point of view. His conclusion regarding the whole army, and for the Bavarian contingent in particular, was "that the civil population was everywhere better off than the army, with respect to mortality from tuberculosis," so that it is hardly conceivable that tuberculosis was introduced among the military by the civilian recruits. Since we are dealing with selected individuals, who, *à priori*, should not be predisposed, the greater frequency of tuberculosis has been variously ascribed to the excessive exertions and hardships of the military service, to carrying knapsacks, to insufficient nourishment, to a completely altered mode of living, and, according to some authors, *e. g.*, Finkelnburg, to homesickness.

A critical study leads to other conclusions. The different armies show the following distribution of tuberculosis:

	AVERAGE YEARLY STRENGTH.	NUMBER OF CASES OF TUBERCULOSIS.	PER 10,000.
Prussian Army (1874–1894), 20 years......	7,593,024	24,012	31.7
Bavarian Army (1874–1894), 20 years.....	967,000	2,690	39.5
Austro-Hungarian Army * (1873–1892), 20 years	5,396,126	30,487	56.5
Belgian Army (1870–1888), 19 years......	791,175	3,924	49.6

We do not know the number of those taken sick among the civil population; but since the yearly number of deaths remains approximately the same, the number of those yearly taken sick (practically the fresh recruits to tuberculosis) must evidently preserve the average. Their number, if we consider the different age-classes and place the average duration of tuberculosis at three years, must correspond to the mortality of that age-class which is three years in advance. According to our tables, therefore (page 249), at the age of twenty, about 84 are taken sick in every 10,000.

In the army the cures, which occur more frequently on account of the early recognition of the disease, are also added, and cases of re-infection, which are counted as double, would have to be subtracted.

Therefore, since in Prussia if of every 24,012 cases of tuberculosis

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* The figures of the Austro-Hungarian army have reference to the number of men treated. This figure, since the number of sick from the preceding year is added, is greater than the number of those taken sick, in the proportion of 100 : 95.

3225 were cured, we should have to diminish the number of the diseased by 4.25 per 10,000 for purposes of comparison with the civil population; this would give us the figures 27.5 instead of 31.7.*

If we divide the average three-yearly duration of tuberculosis into six semi-annual divisions, the conditions would be about as follows: Of the infected and in part already consumptive individuals (84 to each 10,000 of the same age) who present themselves annually for military duty, those who are in the last half-year of the disease, and are therefore near death's door (namely, 0.14 per cent.), are not even ordered to report, on account of their serious illness; those who are in the third and fifth semester of the disease (*i. e.*, three-sixths, or 0.42 per cent.) are recognized as being tuberculous and refused; the remaining two-sixths (*i. e.*, 0.28 per cent.), who are in the first and second half-year of the disease, are for the most part not diagnosed.

Those who are judged serviceable, among whom there are about 0.28 per cent. cases of latent tuberculosis, remain under the same conditions for about another half-year before entering upon their service, and are therefore subjected to the same dangers of infection as those of the same age who are unfit for service. The number of persons infected in six months (0.14 per cent.) must, therefore, be added to these.

There ought, then, to be 0.42 per cent. persons already infected with tuberculosis among those commencing their military duty in the fall. For the most part, the tuberculosis is still latent, and in the different stages of development in the following proportions: 14 being in the first, 14 in the second, and 14 in the third half-year of the disease. Those who are in the fourth half-year of the disease, namely, 28, will show clear signs of tuberculosis after one or two half-years of service, whereas those who are in the first half-year of their infection will become sick only during the second year of service.

A corroboration of the accuracy of our observations is furnished by the circumstance that the frequency of tuberculosis in the army diminishes with the duration of the service, whereas, on the supposition that predisposition constitutes the important factor, more and more individuals ought to succumb to tuberculosis with the increasing length of service, the overexertion, etc.

Eight hundred and forty-two cases of pulmonary consumption and hemoptysis occurring in the Bavarian army† in 1890–94 are divided as follows: For the first half-year, 37.2 per cent.; for the first year of service, 53.4 per cent.; for the second year of service, 22.2 per cent.; for the third year of service, 14.4 per cent.; for the fourth year of service, 10.0 per cent.

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* In Bavaria 166 out of 2690 sick were designated cured.

† I have not been able to obtain any data on this subject regarding the Prussian army.

There can be no doubt, therefore, that a number of consumptives, or of individuals infected with tuberculosis, enter the army, and that the military service as such, in spite of the greatly increased demands on the organism, cannot be held responsible for its occurrence. In fact, the decrease in the number of those taken sick during the second year of service, which becomes still more marked in the third year,—with the former service of three years and the falling-off in the number of new cases which are due to occur at that age,—almost seems to indicate that the same age-class in the army enjoys a greater immunity from infection than the corresponding class of civilians.

This protection, it is true, is not absolute, for cases of infection undoubtedly occur in the army, especially when the hygiene of the barracks is faulty. Formerly, when barracks-life was equivalent to crowded living and uncleanliness, infection probably occurred very often, and it may still do so in some armies. It is possible, also, that the quartering of soldiers on citizens, as during maneuvers, furnishes considerable opportunity for infection. But then as a compensating factor there is the extended stay of the soldiers in the open air, which we do not find among civilians of the same age.

A causal relationship between tuberculosis in the army and the so-called ill effects of military service, overexertion, etc., cannot, therefore, be supported.

For the same reasons, tuberculosis does not become more prevalent during wars, in spite of the fact that soldiers are exposed to the greatest bodily hardships conceivable; to insufficient nourishment, to sudden climatic changes, and to the cold and wet of the bivouacs. In the year 1870–71, when the Germans had 1,000,000 men in the field, who were less carefully selected than in times of peace, 1630 all told died of consumption in the two years, so that, even granting that some succumbed to the disease later on, we are not justified in speaking of a noticeable increase, such as one would be led to expect. In contrast to this, the French prisoners of war in Germany, "who led a regular and restful life" (Guttstadt), showed, according to Kelch, a considerable mortality from tuberculosis, which finds its natural explanation in the crowded manner of living.

Tholozan reports that tuberculosis scarcely occurred in the army besieging Sevastopol during the winter of 1854–55, in spite of the great hardships, frequent night watches, insufficient clothing and food, and exposure to cold and wet.

Alcohol and Tobacco.—Certain authors (Kroczak, Mackenzie) believe that alcohol predisposes to consumption; Kraus, in Lüttich, and Launay and Lanceraux that it hastens the course of the disease. In certain temperance pamphlets, which generally blame all the vices and weaknesses of the human race to the abuse or even the use of alcohol, we find tuberculosis mentioned as among the commonest results of alcoholism. Other authors, again (Meyerhoff, Peters and Jackson), did not find many alcoholics among the consumptives; and it is not so long ago that certain physicians kept their consumptive patients mildly intoxicated, and claimed beneficial results. A numerical demonstration that the abuse of alcohol predisposes to consumption does not yet exist.

The same may be said of tobacco. About twenty years ago smoking was included in the category of factors predisposing to consumption. At the present time consumptives are allowed to smoke moderately, provided they have no throat symptoms. All these habits when followed to excess are harmful only indirectly, by diminishing the nutrition.

Occupation.—Persons following certain of the trades show greater susceptibility, so that tuberculosis occurs fairly frequently among them even with apparently insignificant opportunities for infection. As an example we have stone-cutters, whose lungs are irritated by the sharp dust-particles. The accumulation of this dust forms a caput mortuum in the bronchioles, from which bacilli are only with difficulty carried away. In spite of the fact that these people spend the greater part of the day in the open air, they frequently become infected in the short time which they spend with consumptives in taverns, as well as during the winter, when they follow a different employment.

In most trades the increased frequency of tuberculosis is not to be ascribed to a greater susceptibility, but, as has already been mentioned, to the increased exposure which is brought by work in small dwellings and in a dust-laden atmosphere (see page 268 seq.).

DISEASES.

During the past a great number of diseases have at one time or another been considered as predisposing to tuberculosis, and again as possessing immunizing powers. All these statements must be accepted with the greatest caution. In the first place, they are frequently based on the experiences and impressions of single individuals; secondly, where figures are furnished they are much too small for statistics; thirdly, insufficient care is taken to ascertain the relative number of those who die at the same age of tuberculosis, though not suffering from the other disease.

Diseases of the Blood and Heart.—In case of anemia and chlorosis, which are also regarded as predisposing causes, we are generally dealing with the result of tuberculosis. On the other hand, a great number of people who have always been pale remain well, whereas numerous robust people are carried off by the disease.

Others, again, attach importance to the narrowness of the aorta; Brehmer attributed the development of consumption primarily to the influence of a small heart and the disproportion between it and a large lung; this hypothesis is also open to criticism.

On the other hand, a certain protection is credited to marked valvular lesions. This has been explained by the stasis occurring in the pulmonary vessels. For the same reason, a kyphosis is considered to a certain extent as a protection. Birch-Hirschfeld found chronic pulmonary tuberculosis 907 times, or 20.8 per cent., in 4359 autopsies; in 107 autopsies on cases with lesions of the heart-valves, 5 times, or in 4.6 per cent.; on the other hand, two cases with stenosis of the pulmonary valve showed a pulmonary tuberculosis.

Concerning the favorable influence which is perhaps exercised by a venous stasis in the lungs, see under Chapter III, Part II, "Course."

Diabetes; Malaria.—Among the constitutional diseases which are believed to predispose to tuberculosis, diabetes, which is generally associated with a diminished activity of the heart and skeletal muscles, holds the first place. The pulmonary changes occurring in diabetes were formerly considered to constitute a special form of phthisis until von Leyden, Riegel, Immermann and Rütimeyer, by demonstrating the presence of the tubercle bacillus, determined its identity with pulmonary tuberculosis. Here we may properly speak not only of a greater susceptibility to infection, but also of a better soil for the growth of the bacillus, since it is well known that the addition of sugar to culture-media produces a more abundant growth of the bacillus. According to Germain Sée, a fourth (23 per cent.) of the diabetic patients die of phthisis. This is very questionable evidence, it is true, since the ratio of the percentage of deaths from tuberculosis to the general mortality is very great at the age in which diabetes occurs.

According to some authors, malaria also produces predisposition.

Psychoses.—The frequent occurrence of tuberculosis in sufferers from psychical disorders, especially in those forms characterized by deep depression and an apathetic stupor, associated with a reduction of the vegetative functions, can be explained by the reflex excitability to inspired particles of dust. Moreover, the opportunities for infection are considerably increased in an asylum, through association with consumptive inmates; the insane, who spend most of their time outdoors, suffer less from tuberculosis (see page 272).

That, in addition, predisposition exists in the true sense of the word, namely, that the soil is more favorable, has not as yet been proved. The chief cause of the increased mortality from tuberculosis does not depend on these circumstances, but rather on the opportunities for infection in asylum life, as is shown by the marked decrease of tuberculosis in the Prussian insane asylums since prophylactic measures were introduced.

Defects.—All solutions of continuity of the skin and mucous membranes, wounds of any description, either accidental or surgical, which facilitate the entrance of the bacillus, act as predisposing factors in a local sense. As such, we recognize fissures of the skin and mucous membranes, rhagades (tuberculosa cutis verrucosa), bites, scratches, penetrating wounds at autopsies, insect-bites, tattoo marks, vaccination wounds, abrasions from pointed prominences of teeth, extractions of teeth, burns (skin, tongue), burns from caustics (esophagus), wounds of the navel (peritoneal tuberculosis), abrasions from hard fecal masses (rectum), digging in the nose with the finger, puncturing the ears for rings, irritation from contact of different parts (processus vocales), injury of the eye (iris-tuberculosis from straw, etc.), abrasions of the genitals from foreign bodies, and bites of lice, etc.

Depending on the experiments of Celli and Guarnieri, who were able to obtain positive results from the inhalation of dried pulverized sputum only after previously irritating the respiratory passages of animals, some authors believe that this is a *conditio sine qua non.* This is incorrect, as the thousands of experiments on animals made by other scientists (to which may be added 3000 experiments of the author) prove conclusively, since even through the uninjured skin and mucous membranes tuberculosis was regularly produced by trituration, overfeeding, or insufflation of infectious tuberculous material. The sources of error leading to the contradictory results of Celli and Guarnieri and others have been pointed out above (see page 101).

Inflammations; Catarrhs.—Diseases of the skin, *e. g.*, eczema (see page 116), catarrhs (bronchitis, pneumonia), act in the same way as epithelial defects in favoring the localization of the bacillus. There is a difference, however, that the profuse secretion serves in turn to eliminate the bacilli, a fact which accounts for the antagonistic observations of different authors.

Trauma.—In discussing infections of the pleura, bones and joints (see page 232), and of the brain (see page 234), it has already been explained how a trauma produces tuberculosis of these organs. In the same way, such traumata, acting either directly or by contrecoup on cheesy bronchial glands, or on a tuberculous focus of the lung, may produce an infection of the lung, or, if the bacilli enter the circulation, of any other organ. Naturally, the bacilli are deposited wherever the destruction of blood-vessels arrests their further progress in the circulation. Traumatic tuberculosis of this sort has been discussed in detail by Mendelsohn, Guder, Grawitz, and lately, in a very excellent dissertation, by Reinert. The misconception that in such cases bacilli circulated in the blood from the start and waited as it were for a trauma, for a chance to get a foothold, has been already refuted in another place.

Syphilis and Gonorrhea.—Taking the standpoint that any injury facilitates the entrance of the tubercle bacillus into the tissues, one may also regard syphilis as a factor favoring tubercular infection. Combinations of both diseases, either the localization of the tubercle bacillus on a syphilitic focus or the reverse, are not infrequently observed. I refer to the cases reported by Hiller, de Renzi, Massei, Grünwald, Arnold, Agnanno, Elsenberg (secondary tuberculosis), Helwes, Irsai, Schuchardt, Fabry (of the prepuce), Besnier (syphilis and lupus especially of the throat and larynx), Guidone, Rieder (of the rectum), and Potain. Now and then we have to deal with manifestations of tuberculosis in syphilitic individuals which have no causal relation to their lues. It has been observed that gonorrhea favors the occurrence of tuberculosis of the testicle (Simmonds, Karewski), the urethra (Ahrens), the kidney, etc.

Carcinoma.—The same holds good for carcinoma. Here also we may find a symbiosis of both processes in the various organs. Such cases have been described by Lewin in the skin, by Zenker and by Cordua in the esophagus, in the larynx also by Zenker, of the ileum by Lubarsch, of the rectum by Baumgarten, of the auricle by Haug. Whereas, in these cases, the tubercle bacillus apparently entered through the epithelial defects produced by the cancer, we also find carcinomatous degeneration of tuberculous foci, especially in areas of lupus. Additional cases may be found in the writings of Lewin, Friedländer, Weber, Pick, Volkmann, Krone, Schütz, Nielsen, Hebra, Desgrave, Kenibaschieff, and others.

Typhoid.—Mosler and others have called attention to the localization of tubercle bacilli in typhoid ulcers.

All these cases evidently do not depend on any alteration of the soil on which the bacillus grows, but on the greater ease with which they secure a foothold. That this is so is proved by the fact that the bacillus does not become localized anywhere in the body except where the portals for infection are open.

The observation that previous cases of typhoid often return to the hospital in a short time with pulmonary tuberculosis can be explained by an infection occurring during their first sickness.

Measles, Whooping-cough, Scarlet Fever.—A certain group of infectious diseases, in all of which the respiratory organs are particularly affected, is held especially responsible for the occurrence of tuberculosis. These diseases are measles and whooping-cough, and, in a lesser degree, scarlet fever and diphtheria. The influence is of a double kind. These diseases are associated to a great extent with irritation of the mucous membrane and defects in the epithelium, and in this way facilitate the entrance of the bacilli, so that infection of the respiratory passage is particularly favored.

Furthermore, they are associated, as a rule, with a more or less marked swelling and infiltration of the glands, especially the bronchial glands. If, as is generally the case, these glands already contain a small tuberculous focus, the capsule bursts and an emigration and mobilization of bacilli occurs. These become localized either in the adjacent part of the lung (hence the favorite location at the hilus) or in any other part of the body, if they enter the circulation (meninges, bones, etc.). In this way the frequent evolution of pulmonary tuberculosis, miliary tuberculosis, etc., from a latent focus, as a sequel to the previously mentioned diseases, is explained. Whether these diseases have been responsible for a real infection, or only for the dissemination of a latent tuberculosis, can be deduced to a certain extent from the time of appearance of the manifestations. If the latter is the case, the symptoms of tuberculosis appear almost immediately (or a few weeks) after the previous disease, since a large number of bacilli are at once drawn into the organism; on the other hand, with a primary infection the symptoms appear only after months. If such patients are brought to us early enough the presence of cheesy glands can be frequently determined (Marchand). Tuberculosis as a sequel to these diseases is observed most frequently in scrofulous children and those of tubercular parentage (opportunity for infection). Tuberculous disease of the middle ear, also, which appears to light up especially after scarlet fever (otitis suppurativa scarlatinosa), may be similarly explained.

Influenza.—When at the end of the last and at the beginning of this decennium influenza spread through the country, pulmonary consumption was reported by many as following upon this disease. In by far the greater number of cases the cause must be sought, not in the favorable conditions for a primary infection nor in an increased predisposition, but in the dissemination of bacilli from a preëxisting though possibly latent focus in the lung. This may be due to the secretions of influenza or to the mobilization of bacilli embedded in the glands. That tubercular infections have not been increased by influenza may be deduced from an article by P. Sperling, in which he shows that the mortality from consumption was not noticeably increased during that period, but merely that the course of the disease became more rapid. Similar results were obtained in statistics on influenza in Massachusetts.

Whether any of the previously mentioned diseases alter the reaction of the organism to the tubercle bacillus has been, if we except diabetes, neither proved nor investigated. Nor are we able to determine whether these diseases are capable of producing an indirect effect, by weakening the ciliated epithelium of the bronchial tree. The removal of the bacilli would undoubtedly be accomplished with greater difficulty if this were actually the case, but our knowledge regarding this particular point in the pathology of these diseases is unfortunately almost a blank.

Part II.

PULMONARY TUBERCULOSIS.

CHAPTER I.

PATHOLOGICAL ANATOMY.

GENERAL PART.

The most superficial inspection of the body of a person who has succumbed to pulmonary tuberculosis gives an appearance in many ways so typical that the diagnosis may be made at once. The body wasted to the bone, the hollow cheeks, the sunken eyeballs, the everted ears, the bony prominences of the hips and buttocks, the characteristic skin, pale, bloodless, often even grayish in color, wrinkled and folded, covered, especially over the chest, with scales and pityriasis versicolor—all these declare the terrible scourge. On the other hand, we are not infrequently confronted with well-nourished bodies, presenting a fair development of the subcutaneous fat, a powerful musculature, and a florid appearance even in death, yet the lungs give evidence of widespread disease.

PULMONARY CHANGES.

The pathological changes in the lungs can be understood only after an investigation of their developmental phases. Tuberculosis of the lungs is traceable etiologically to infection by way of the blood, lymph, or air-passages. If the blood-channels be all at once flooded with bacilli, by the rupture of some tubercular focus in the body, then, corresponding to the amount and wide distribution of the infecting agent, there results a diffuse miliary tuberculosis of both lungs, which forms part of the picture of a generalized miliary tuberculosis.

The lymph-paths are invaded by bacilli from neighboring tubercular foci, such as a carious vertebra or rib, or, with special frequency, a tubercular bronchial gland of which the capsule has ruptured. Taken up by the lymph-stream and the lymph-spaces of the tissues, these bacilli are deposited in various spots, and produce either miliary tubercles or larger nodules, whose source is distinctly indicated by their radial distribution from the common center of origin. Since, in such cases, the invasion of the bacilli forms a succession of events, the peripheral nodules are found to be smaller and younger than those nearest to the "mother-focus."

But infection by the air-passages plays by all odds the most important rôle in the production of pulmonary tuberculosis. This method of invasion must be taken to include a rather infrequent occurrence, namely, the rupture of a tuberculous focus into the bronchi or trachea, and also, at times, the aspiration of cheesy masses derived from an ulcerating tubercle of the larynx, tonsils, or nasopharynx. Yet these accidents are rarities, and the important factor in the infection of the lungs is, without any doubt, the inspiration of tubercle germs from the atmosphere. In the vast majority of cases, doubtless, one single germ, or a single group of germs, enters in this manner, a fact of which we may feel well convinced when we consider the mere physical obstructions to the entrance of dust-like particles into the normal air-passages. Nor is our conviction shaken by the greatly exaggerated accounts of the vast numbers of bacilli contained in the atmosphere about us.*

Primary Localizations.—There is a general agreement with the theory of Rindfleisch, that the site of the earliest changes in pulmonary tuberculosis is at the transition from the ultimate bronchioles into the alveoli. It is going too far, however, to set this up as a universal rule. There is, indeed, no ground for denying that the tubercle bacillus, which at times travels from the mucosa of the bronchioles to the bronchial glands without producing any alteration, may be deposited at any point along this course and undergo the characteristic developmental changes. Thus it might lodge within the bronchioles, or directly in the alveoli, or again in the lymph-channels leading from these. Just such a distribution is illustrated by Arnold's experiments with inspired particles of coal-dust, which could later be traced to every possible point in the lung. Moreover, in the artificial production of tuberculosis by inhalations the tubercles are found variously located; but whether the inhaled bacteria become deposited in the bronchioles, or in the alveoli, or in the interstitial tissue, they always produce those characteristic alterations which we have described as the histogenesis of the tubercle. They induce proliferative activity on the part of the epithelium and the fixed tissue-cells, and an inflammatory invasion by leucocytes, with eventual caseation. The pulmonary tubercle is in all essential particulars a duplicate of the tubercle in other organs of the body.

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* The question is different when the individual is exposed to an extraordinarily heavily infected atmosphere, as in the well-known case of Tappeiner's assistant, cited by Schweninger. This man, who was healthy, very powerful, and had no hereditary predisposition, could not keep away from a room in which some dogs were being exposed to the inhalation of tubercular sputum. He succumbed very shortly to the disease, and had the same multiple foci in his lungs as the animals which were subsequently autopsied.

Fate of the Tubercle.—*Fate of the Primary Tubercle.*—If, now, the tubercle which has thus arisen is successfully isolated by fibrous encapsulation, there arise no consequences of moment to the organism; but if the attempt to wall it off be inefficient, the bacilli multiply with enormous rapidity, and some migrate radially into the surrounding tissues, spreading the infection on every side, both through the air- and lymph-channels, and also by continuity. The repetition of the same process results in the production of one or more isolated or conglomerated tubercles, the cheesy centers may become confluent, and thus a cheesy nodule of variable size may be formed. (Tubercular alterations in the lungs, especially such as are characterized by caseation, ordinarily go by the name of pulmonary phthisis, or simply "phthisis," since other pathological processes so rarely produce these changes that they may be practically ignored.)

The Cheesy Nodule.—The cheesy nodule may also become encapsulated, especially if it has not already reached too great a size. In that case it may remain isolated, its cheesy contents may, by the deposition of lime salts, become chalky and calcified, the bacilli ultimately become annihilated, and so, in a word, a species of cure be accomplished. Or, the cheesy, infected contents soften, burst into an open bronchus, and can be thrown off with the normal or pathologically increased secretion. If the evacuation of its contents be fairly complete, the cavity of the nodule becomes gradually filled up by granulation tissue; it continues to secrete for some time, yet slowly cleans up, and the process of cicatricial contraction begins; eventually the walls come into contact, unite, and a smooth, tough scar is all that remains. The traces of such a process are not infrequently to be found in the bodies of persons who show no other sign of tuberculosis.

Unfortunately, however, the outcome is not, as a rule, so favorable as has been portrayed in either of the above forms of termination of the tubercle. For it happens not infrequently that the fibrous capsule is not sufficiently resistant, or is too slowly developed, and that some of the tubercle bacilli, which are most densely packed at the periphery of the nodule, pierce its wall and distribute themselves throughout the organism. It is just in this manner that the bacilli force an entrance into the bronchioles, or into the rich lymphatic capillary system of the lung, and so establish new foci of infection.

Furthermore, the cheesy content of the nodules, which is always laden with germs, is not invariably expectorated and lost without effecting further consequences to the organism. In the first place, the proteins and the metabolic products of the bacteria, which give the cheesy matter a peculiar chemical make-up, act as irritants to the bronchial mucosa, and produce hyperemia and mucous catarrh. This facilitates expectoration very materially. But, on the other hand, with every fairly deep inspiration small particles of the mucoid material are carried into other parts of the lung which were previously healthy. The areas bordering upon the primary focus are first subject to infection in this way; but even distant parts, the bronchi of the opposite lung, for example, are not exempt. It is undoubtedly true that succeeding expiratory efforts will result in the expectoration of a portion of the infectious material, but the residue remains, especially in the bronchioles and alveoli, and inaugurates a fresh series of pathological changes. Very large areas of the lung may become simultaneously affected in this way.

The pathological changes in the lung exhibit a remarkable diversity, depending upon several factors, namely, as to whether the bronchi or the lymph-vessels act as the channel of infection, whether living or dead bacteria with their proteins and toxins are the infectious agents, and whether few or many bacteria are involved.

As a general rule, bacteria coming from the periphery of a cheesy nodule are still living, and produce changes of a proliferative type; moreover, they invade the lymph-channels in small numbers, and so give rise to isolated lesions. On the other hand, bacteria coming from the center of old cheesy nodules are for the most part dead, the poisonous products of their bodies, the proteins, have been absorbed, and they produce changes preëminently exudative in character, although stray bacteria, which have retained their vitality, occasionally set up a proliferation. Infection through the bronchi and the sputum produces an actual inundation of the tissues, which again sets its stamp upon the character of the change. The various forms of pathological changes, depending upon the nature of the infective material and the mode of infection, are not always sharply distinguishable, and often occur associated in the same lung. Nevertheless two main divisions can be made, namely, tuberculous peribronchitis and cheesy pneumonia, to which a third form, comprising those processes which are due to a combination of tubercle bacilli with other forms, the "mixed" or secondary infections, may be added.

Tuberculous Peribronchitis.—The tubercle bacilli which have gained entrance into the lymphatic system are washed into the lymph-channels which accompany the bronchi and blood-vessels (perivascular and peribronchial lymph-channels), and lodge here for longer or shorter periods of time, giving origin to fresh processes. Along the course of the vessels and the bronchioles a perfect series of tubercles is formed, which often covers a long stretch of lung-tissue. The nearer this chain is traced to its origin, the older and more perfect are the tubercles. Apparently the infection may at times travel against the direction of the lymph-current, a fact which may be explained by the alteration and reversal of the current through blockage. The condition of the lungs thus set up is known as tuberculosis peribronchialis and perivascularis, or, if the inflammatory reaction be very intense, as peribronchitis tuberculosa (lymphangitis and perilymphangitis tuberculosa).

The favorite seat of these tubercles is at certain points of intersection of the finest lymph-spaces, as at the transition of the alveolar passage into the bronchiolus; this they actually engirdle, so that its lumen forms a slit-like passage through the tubercular mass. If a number of bronchioles become involved, "clover-leaf" areas are formed. If the bacilli gain a foothold in the lumen of a bronchus or bronchiole, they set up a tuberculosis bronchialis, or a bronchitis tuberculosa, either of which may become the starting-point of a tuberculous peribronchitis.

Each of these foci may go through the entire cycle of development with all its concomitants—becoming caseous, fusing with other caseous nodules, and constituting a center of fresh distribution.

Cheesy Pneumonia.—In contradistinction to the above process, which involves principally the interstitial and interalveolar portions of the lung, we find that aspiration of the infectious material through the bronchi produces the most important changes within the alveoli and the bronchial mucosa. The matter so aspirated is, as a rule, very rich in proteins, and, as a consequence, the inflammatory and exudative reaction is strikingly pronounced. Cheesy pneumonia, or bronchopneumonia, results, which anatomically is sharply distinguishable from peribronchitis. If the inspired masses lodge on the mucous membrane of the bronchi or bronchioles, without penetrating to the alveoli, a bronchitis caseosa results, followed by bronchiectasis. If the caseous pneumonia is limited to single alveoli, the small foci, which often encircle the terminal bronchiole like a crown, simulate miliary tubercles (miliary cheesy pneumonia). If they embrace a lobule (lobular cheesy pneumonia), they appear distributed over the lung as small cheesy islets, surrounded by an inflammatory zone. When the islets lie close to one another over a wide area, the cheesy pneumonia may appear to be lobar. Since various lobules are not always involved simultaneously, but often in succession, several stages of development are found associated.

The beginning of cheesy pneumonia is characterized by the formation of a viscid, transparent exudate, rich in albumin and especially, as Orth has shown, in fibrin. At the same time, there is an active proliferative process, with an exfoliation of the epithelium (hence the "desquamative pneumonia" of Buhl), and an exudation of cells consisting of leucocytes and erythrocytes. With the further development of the process these pathological products undergo caseation (cheesy hepatization).

The cut surface is at first grayish-red, later yellowish-white; it is opaque, nodular, and dry, seems airless, and resembles the cross-section of a so-called "country-sausage." If the process goes on rapidly to softening, caseation, and destruction, it is known as phthisis florida.

[The various forms of tubercular inflammation of the lungs show an essential unity. There is a growing tendency to do away with the more elaborate classification of the varieties of the lesion. Baumgarten* in a timely utterance maintains this unity, and denies that there is any essential structural distinction between caseous pneumonia and miliary tuberculosis of the lungs. The difference between them is chiefly quantitative, not qualitative. Both pathological processes as described occur to some extent in each of these forms of tuberculosis. Caseous pneumonia is not merely an intra-alveolar exudation, nor is miliary tuberculosis simply an interstitial proliferation. On the contrary, both processes are present in each case, though in varying proportions.—Ed.]

Gelatinous Infiltration.—There is still another characteristic form which differs in several particulars from the ordinary type of a cheesy pneumonia. The picture is modified by the formation of an exudate, either serous, gelatinous, or occasionally fibrinous, in great quantity, while the proliferation and desquamation of alveolar

* Deut. Arch. f. klin. Med., lxxiii, 1902.

epithelium becomes much restricted. This exudate, involving large areas of the lung, is either homogeneous throughout, or encloses numerous larger or smaller foci of marked proliferative activity. This form of the disease, known as gelatinous infiltration or smooth ("glatte") pneumonia, has been studied with especial care by A. Fränkel and Troje, who find that tubercle bacilli are practically always absent, and that other forms of bacteria also are rarely found in portions of lung so affected. It differs, further, from caseous pneumonia in its course, since it does not necessarily go on to caseation, but may undergo retrogressive changes and absorption. It owes its origin chiefly to the aspiration of material from old cheesy foci in which the bacteria have for the most part gone to pieces, while their proteins are so much the more abundant. With this origin corresponds the total absence of bacteria in the product. If, however, the aspirated material contains still living bacteria, these naturally go on to development and give rise to the cheesy islets which form the transition to an ordinary cheesy pneumonia.

Mixed Infection.—Finally, the pathological processes are altered by the presence in the tubercular areas, especially in cavities, of other species of pathogenic bacteria. These are, according to the findings of the author, preëminently streptococci, less frequently the pyocyaneus, pyogene saureus, etc. These organisms not only vegetate upon the excellent nutritive medium, but also take an active part in the further development. This is demonstrated by their position in the walls of cavities, especially in cases of rapid disorganization, in which they may be seen to follow the tubercle bacilli at every step, and even to lead the advance. This secondary invasion of bacteria is capable of producing and maintaining suppurative processes, and so greatly accelerates the destruction of the lung, as is evidenced by the cases of phthisis florida. Moreover, they are carried into a previously healthy lung, and at times produce fresh pneumonic infiltrations, which differ from the gelatinous areas by being less transparent. (A. Fränkel and Troje. See, further, chapter on Complications.)

[The study of the associated infections in pulmonary tuberculosis is becoming more and more important. Sata * and Ophüls † and Weismayr ‡ have investigated this question, and their conclusions are for the most part in accord. While cavity formation can probably go on in the presence of the tubercle bacillus alone, yet in most cases there is infection with one or often more varieties of bacteria. Pulmonary phthisis is a pure infection with the tubercle bacillus only in the early stage. Later only cavities completely closed off remain free from infection with other bacteria. The immediate influence of the secondary infection upon the lung lesion is of two kinds: First, to increase the tendency to tissue destruction, and make it more rapid; second, to bring about pneumonic consolidation, in which these secondary bacteria are generally found in large numbers. It must be remembered, however, that Ophüls has found a number of pneumonic lesions in which only tubercle bacilli could be made out. The commonest form of mixed infection is with Streptococcus pyogenes; less often there are found staphylococcus, pneumococcus, colon bacillus, tetragonus, and the "pseudo-diphtheria bacillus pulmonalis" and the influenza bacillus. In many cases several of these bacterial forms are present. Weismayr found a secondary infection in all his cases of complicating laryngeal tuberculosis.—Ed.]

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* Ziegler's Beiträge, 1899, supplement heft.

† Am. Jour. Med. Science, 1900.

‡ Zeitschft. f. Heilkunde, Bd. xxii, 1901.

Subsequent Fate of the Tuberculous Focus.—The further course of the peribronchitic tubercle and of the cheesy infiltrated areas is identical with that of the primary foci. Tubercles and cheesy foci of small extent are frequently shut off by fibrous encapsulation, and may eventually become chalky and calcific. As long as cheesy masses remain, they continue, apparently, to be a source of danger. Now and then the lime-concretions are dissected off, sequestrated, and thrown out in the sputum ("lung stones"). Fibroid proliferation, as already described in the encapsulation of the primary tubercle, plays an important rôle in the cure of tubercular processes. It consists primarily in an indurative inflammatory process, which starts at the circumference of the caseous focus; while the induration involves the intervening lung tissue between single foci, often atelectatic through the plugging of the afferent bronchus, it may eventually embrace wide areas, especially at the apex (apex induration). Thus it may metamorphose considerable portions of lung into cicatricial fibroid tissue, laminated and of a gray-blue color, in which the cheesy and calcareous foci lie sprinkled. In proximity to these indurated cicatrices there is often a complementary emphysema. Induration processes such as these are especially associated with disease of a chronic type, to which, indeed, they partly lend this character, inasmuch as they constitute a sort of curative process.

If the caseous foci be of greater extent, the course is somewhat different. Softening and liquefaction progress from the periphery to the center, often with the coöperation of pyogenic bacteria, and eventually there is formed a cavity, walled off and surrounded by caseous material, known as a vomica. Sooner or later the softened masses force an entrance into one or more bronchi, and are thus evacuated. The advantage to the organism of ridding itself of all this infectious and poisonous material is evident, but is somewhat offset by the imminent danger of a fresh aspiration which is thus induced.

In case the evacuation of the cavity is perfect, the walls become cleaned up by exfoliation of the cheesy detritus, and by the formation of a granulation tissue which is richly vascularized and prone to bleed. The surrounding tissues may also take part in this process of induration, and thus, relatively speaking, a cure is accomplished. Pathologically, either one of two conditions will be found to exist. In the first place, the walls may become approximated and cicatrized, thus giving rise to a characteristic contraction and puckering of the lung tissue often evident even at the surface. Or, in cases in which the cavities are of large size and their walls held rigid by inflammatory adhesions, as frequently in apical disease, a cavity results of which the size varies from that of a pigeon's to a hen's egg or even greater. When the process has this latter termination, the organism is always threatened with the danger of suppuration or even of gangrene in these cavities, which may have the most serious consequences. Such a danger is always present even if the bacteria are all dead.

In another type of case the destructive progress of the disease is absolutely irresistible, or meets with only a localized and inadequate defense. Neighboring cavities become confluent and form an irregular labyrinth with many chambers, traversed by numbers of buttresses and partitions, the relics of the broken-down tissue. The walls become ragged and broken down. The caseo-purulent contents become gray, grayish-yellow, or brownish, and are composed, among other things, of elastic fibers, which have been set free by the destruction of the alveolar framework, also of innumerable tubercle bacilli, and of white clumps, which often contain the bacilli in pure culture. Often enough other bacteria are to be found, such as S. pyogenes, the usual pyogenic organisms, diplococci, etc. The tubercle bacilli are most numerous in fresh, cheesy foci and in the walls of cavities which are undergoing rapid demolition; they are infrequent or absent in cicatricial, shrunken, pigmented tissue.

At times, almost the entire upper lobe and a considerable portion of the lower fall a pray to the swift process of destruction, and cavities as large as a fist are no rarities. It is significant that the wall of the cavity gives evidence very often of a localized curative effort, as is shown by the indurated character of considerable portions, and their comparative freedom from bacteria, while in another corner or recess are to be found entire colonies of bacteria, with all the signs of advance. This fact, that in the same individual one and the same lobe of a lung, nay, more, a single focus, may at one and the same time contain certain areas almost perfectly healed, other areas undergoing gradual destruction, and still others showing rapid dissolution, hardly serves to support the theory that the body-fluids, which are, of course, uniform throughout, constitute "diathesis" in tuberculosis, or, in other words, are the factor of chief moment in determining whether the body is to be successful in its struggle with the disease.

Tubercular areas at the surface produce irritation and thickening of the pleura, and fusion of the costal and pulmonary folds. This occurs especially in slowly advancing processes. When the caseous focus breaks down with great rapidity, the adhesions may fail to form, and occasionally the external wall of the cavity becomes eroded, the pleura is perforated, and there results an entrance of air from the lung into the pleural cavity. The result is a pneumothorax, or, if the contents of the cavity are also voided, a pyopneumothorax. In order to demonstrate such perforative passages in the corpse, one fills the suspected pleural cavity with water and forces air through a catheter into the trachea. If perforations be present, air-bubbles rise in the water (Kaufmann).

The condition of the vessels demands special consideration on account of the hemorrhages which so frequently interrupt the course of a pulmonary tuberculosis. Lymphatics, capillaries, small blood-vessels in tubercles, and cheesy consolidations early become subject to inflammatory obstruction. The larger vessels, on the other hand, show a thickening of their walls which enhances their power of resistance against the disease. One may assume that this change in the vessels, which is evident also in the immediate neighborhood of cheesy foci, depends upon the chemical irritation of the proteins.

In case living bacilli come into direct contact with the unaltered vessel wall, tubercle formation results, as is evidenced by the presence of closely associated tubercles in the arteries (Orth), but more commonly in the veins (Weigert), in both the acute and chronic forms of tuberculosis. In these cases, likewise, tubercle formation is preceded by thrombosis and blockage of the lumen, which generally serve to prevent the dispersion of the germs throughout the blood-stream.

In the very earliest stages of pulmonary tuberculosis, while there are as yet few proteins and the living bacillus plays the chief rôle, the healthy wall of the smaller pulmonary vessels is apt to become invaded and eroded, giving rise to a hemorrhage, the danger-signal of an incipient consumption. The very same accident may occur later in the disease, when isolated bacteria become transported through the perivascular lymph-channels to the vessels; but, as a rule, the later course of the disease is marked by endarteritis, obliteration of the small vessels, and thickening of the larger ones. This is due to the chemical stimulus of the proteins which abound in the cheesy infiltrations resulting from the aspiration of sputum and of old caseous matter. It is on this account that hemorrhages are rare or altogether absent in the later stages.

When hepatization has given place to destruction of tissue, the resulting cavities are frequently seen to be traversed by large blood-vessels which run from wall to wall like bands of cord; they are for the most part impermeable, but occasionally retain their functions; they may present aneurysmal dilatations, or may project as stumps into the cavity. Eventually, through erosions or circulatory derangements, they may become the source of profuse or even unmanageable hemorrhage.

CHANGES IN OTHER ORGANS.

Of the other organs, the pleura especially is almost invariably affected. Changes may involve either the apex alone or the entire surface of the lung.

The **bronchial glands** are found to be markedly implicated in almost all cases, especially in young individuals. Very early in the course of the disease they are invaded by tubercle bacilli which are conveyed by the lymph-stream. Now and then they present only single caseous foci or points which are barely noticeable, while their size as a whole is about normal. In other cases they may become markedly infiltrated; they may form large bunches or sacs containing a caseous, soft, greasy, grayish-black material, with an occasional lime-concretion.

The **gut** is rarely free from changes, especially in cases of prolonged duration or with large secreting cavities. Weigert found them in 90 per cent., Wesener in 80 per cent., of the cases of pulmonary tuberculosis. They take the form of tubercles, of ulcers, or, finally, of infiltration and caseation of the mesenteric glands. The ulcers are situated principally in the region of the ileum, and run perpendicularly to the axis of the gut.

The **larynx** is involved frequently, perhaps in 30 to 40 per cent. of the cases.

The **tonsils** were found by Strassmann to be tuberculous in thirteen out of twenty-one autopsies on phthisical patients; Dmochowski found in fifteen cases not a single exception.

The **gastric mucosa** is often normal, or anemic, more rarely hyperemic, frequently catarrhal. Schwalbe found in twenty-five cases of phthisis, amyloid degeneration of the stomach in three, fatty degeneration of the glands in nine, cloudy swelling once, frequent examples of catarrhal affections and isolated cystic disease.

Almost invariably there was a proliferative inflammation of the interglandular connective tissue of a variable degree of intensity. There was no constant ratio to be discovered between the symptoms during life and the anatomical alterations.

The **liver** is often in a condition of fatty degeneration, often sharing with the kidneys, spleen, and gut the fate of amyloid degeneration.

Pericarditis may occur, most often exudative in character. Endocarditis is rarer. The **heart** participates in the general emaciation, and is atrophic. The myocardium is soft, pale, and thin, and shows the atrophy and fatty degeneration which accompany the other forms of cachexia. Not infrequently the right side of the heart presents dilatation and tricuspid insufficiency, a condition which is due to the increase of pressure in an anemic and atonic organ. Tubercles in the myocardium are very rare.

The **muscles** are generally atrophic, pale, thin, partly fatty, and, in case death has been preceded by a period of pyrexia, very dry. The microscopic changes have been studied most carefully by E. Fränkel. In the contractile substance are found transverse tears, separation of the sarcolemma, diminution in breadth, and in the muscle-sheath the presence of finely granular, molecular, partially fatty areas. In the most extreme degree of degeneration he found only empty sarcolemma sheaths. The perimysium showed increase of connective tissue and partial pigmentation. The atrophy of the entire muscle is due to a decrease not in the number of muscle-fibers, but in the diameter of the individual fibrillæ. The above conclusions were verified by Posadsky. (On the subject of tuberculous myositis consult Delorme and Reverdin, VII French Surgical Congress.)

In the **brain** there is ordinarily anemia, rarely hyperemia, occasionally meningitis of tuberculous or non-tuberculous nature, rarely pachymeningitis. In the cord there are frequently similar meningeal inflammations.

The **nerves** frequently become the subject of multiple degenerative inflammation (Pitres and Vaillard).

CHAPTER II.

THE SYMPTOMS OF PULMONARY TUBERCULOSIS.

INTRODUCTION.

The clinical pictures which may be produced by tuberculosis of the lungs in different individuals are protean in their variability, and frequently denote a revolution in the entire economy of the body. In order to gain a closer insight into the changes which the body undergoes, we shall attempt to follow them, and explain their origin, from the first expression of the disease, the tubercle.

The difficulties which beset the invasion and localization of tubercle bacilli in the lung are so great that as a rule only one bacillus, or at least an isolated colony of bacilli, forms the point of departure of the disease. Since, as we know, the single tubercle demands for its complete evolution a certain length of time, about two to four weeks, the early period of infection could hardly be expected to produce any symptoms. In the usual forms of pulmonary infection there is, as a rule, either one focus or isolated foci. Not before these have broken down, when the bacilli have distributed themselves further and further in the surrounding territory, and have established fresh foci, do the first clinical symptoms become manifest. This process may consume months, never less than half a year, occasionally a year or a year and a half, depending upon the virulence of the infection. It is different, of course, in cases where numerous bacilli invade the body simultaneously, as occurs in miliary tuberculosis, with the rupture of some preëxisting focus into the blood-channels. Here, violent symptoms develop as early as three to four weeks after the fatal event, and death ensues frequently inside of another period of the same duration. No matter how sharply localized is the tubercular focus and how closely confined to its own immediate environment, there must always occur, with the breaking down of the tubercle, a diffusion of the soluble proteins. These are carried off by the lymph-stream, invade the blood, reach the various organs of the body, and produce a series of effects which are at first perhaps scarcely noticeable, but which the progress of time tends continually to intensify. These effects are, of course, not uniform, but vary with the quantity of the poison, and with the idiosyncrasy of the individual and of his various organs. It is in the absorption of these proteins, products of metabolism and of disorganization, that one finds an explanation for the constitutional symptoms accompanying a disease which is in itself localized.

The absorption of the poison varies, both with the size and the number of foci. It depends on the surface area of the focus, in such wise that numerous smaller foci afford a larger superficies than single larger ones. It depends, further, on the adjacent tissue, whether this be normal or fibroid, whether its lymph-current be sluggish or active. It varies with the idiosyncrasy of the individual; for example, a young person, with pervious lymph-channels and with an active lymph-current, differs in his absorptive capacity from an older one. The phenomena in the former case are far more acute than in the latter.

At the same time, the disintegration products of the primary tubercle and of the secondary conglomerated tubercles seek an exit from the body. They may find their way into the bronchus; in the early stages, while the bronchial secretion remains almost normal in character, they are with difficulty carried upward, the process being assisted by the ciliary epithelium and forced expiratory movements. The small particles stimulate the mucosa of trachea and bronchi, which are as yet unaccustomed to this form of irritant, producing a dry reflex cough. Eventually they are expectorated, enveloped in a vitreous, scarce altered and hardly increased mucus. Gradually, however, the bronchi lying nearest to the foci of disease respond to the ever-increasing chemical stimulation of the proteins; the mucous membrane becomes inflamed and increases its secretion, especially the formed constituents, the elimination of the caseous material being thus considerably facilitated.

Now and again it happens that soon after the first infection the bacilli erode a vessel-wall, and so produce an hemoptysis, the omen of a future phthisis.

LOCAL SUBJECTIVE SYMPTOMS.

COUGH.

One of the first symptoms of a tuberculous infection of the lungs is cough. It is so constant an accompaniment of this disease that even the laity appreciate the significance of an obstinate cough. In itself, cough is simply a forcible expiratory effort through a closed rima glottidis. It is a reflex phenomenon, inasmuch as the vagus nerve, either the main division or one of its branches, receives a stimulus through the sensory nerves of the bronchial mucous membrane which is carried to the medulla and is there transferred to the motor nerves which control expiration. This stimulus is, in the majority of instances, due to foreign bodies or secretions, and the cough serves the purpose of removing the cause of irritation. Our knowledge of those areas which are especially sensitive to such stimulation is derived from the labors of Kohts, Nothnagel, Störk and Reyher. Most sensitive of all is the interarytenoid space, and next the bifurcation. The tracheal mucosa responds only to rather powerful stimulation. The afferent nerve is the laryngeus superior, which supplies the mucosa with sensory fibers. When the mucous membrane is inflamed, the most insignificant stimuli produce reflex cough.

The cough varies markedly in the different periods of the disease, both in its nature and in its intensity. At first there is only a slight hacking and hawking, which in young people is frequently miscalled a "bad habit." At first this coughing occurs almost exclusively in the morning, later also in the evening, and is associated with the expectoration of occasional small lumps of a clear, vitreous mucus. If the caseous masses derived from the disorganized tubercles succeed in finding their way to the bronchial mucous membrane, they bring about their own ejection in the sputum. Since the mucosa of the smallest bronchi is as yet unaltered and secretes only in very small quantity, these masses come into the very closest contact with it and irritate it both mechanically and chemically. In case expectoration is very difficult, even early in the disease there occurs a dry, violent cough, which often becomes raw and hacking. This cough may be paroxysmal and explosive, and may last a few minutes or half an hour. The face becomes congested, deep red or blue, and the patient is breathless (Stickhusten) and in a sweat; eventually he expectorates a small mass of mucus, which is entirely out of proportion to the severity of the exertion, or he vomits, after which he has a period of rest. Later on, as the irritated mucosa begins to secrete more freely and the expectoration is thus facilitated, the coughing becomes much less severe, though more frequent. It is generally most severe in the morning, owing to the fact that the secretion accumulates during sleep while the reflexes are in abeyance, and in the morning, when they again become lively, demands evacuation. Frequently saliva falls back into the larynx during the night, and the patient wakes in a fit of coughing which often consumes a half-hour to an hour. In many cases the position influences the cough, and many patients are scarcely able to lie on the affected side, perhaps, as in catarrhs, because the increased congestion produces an increase of secretion in the dependent portions.

Coughing depends essentially on the idiosyncrasy of the individual. One will go on for years hardly complaining; a slightly increased expiratory effort, a few short, deep coughs, suffice to throw out the masses of secretion. With another, cough is the most distressing of the symptoms, exhausting the patient by its severity and robbing him of food and rest. Persons of increased irritability, of a nervous and hysterical type, suffer appreciably more with their coughs. In Görbersdorf I observed a hysterical girl with phthisis, who coughed almost uninterruptedly for three weeks, day and night, but with the beginning of the menstrual flow the cough ceased almost completely. The "phlegmatic" individual waits until the sputum comes up of itself; the "choleric" individual attempts to remove the smallest source of irritation by the most violent efforts. Old people cough as a rule very much less. Insane persons, also, especially if the reflexes are diminished, tend to cough little or not at all.

The respiratory mucosa, especially at the sensitive places, the larynx, etc., may be rendered extremely irritable, both through the preceding attacks of cough and by the presence of large masses of sputum rich in proteins. In this condition irritants in themselves insignificant may produce violent cough—small particles of dust and smoke, temperature variations in the inspired air, especially going out-of-doors in winter, going into a warm or cold room, into a cold bed, dry air, cold moist air, a cold drink, bodily exertion which increases the rapidity and depth of respiration, climbing stairs or mountains, loud speaking, laughing, crying, chemical irritants such as alcohol or wine, all have this effect. During the warm season this irritability often almost vanishes. In addition to the usual bronchitis, there is frequently a pharyngeal catarrh, which gives rise, especially in the morning, to incessant hawking, coughing, and even vomiting. Further, there may be a laryngitis, tubercular or not; pleuritic irritability through the presence of superficial tubercles, the normal pleura being incapable, according to Nothnagel, of eliciting cough; finally, there may be enlargement of the bronchial glands with pressure on the vagus. Furthermore, one must keep in mind that cough in phthisical individuals as well as in others may be secondary. The cough of nasal disease is well known (Mackenzie, B. Fränkel, and others); likewise the "ear-cough," which ceases upon the removal of impacted cerumen (Breitung, Jackins); the cough consequent upon ovarian affections (Schnyder, Kurz); the hysterical cough (Strübing, Rosenbach), and the gastric cough.

In conclusion, it may be said that cough gives no true indication of the intensity of the disease, or of its progress, for extensive areas may persist for years and the patient not be seriously incommoded by his cough, while, contrariwise, small changes may be associated with coughing of a violent and paroxysmal nature.

EXPECTORATION.

Expectoration is, in the same manner, regularly associated with pulmonary tuberculosis, but varies enormously during the course of the disease. In the early stages one often fails to make out any increase in the secretion; later on, there is a foamy, viscid, glairy, saliva-like mucus, containing isolated rice-like, firm granules, which are not to be confused with plugs from the tonsils, and dark gray, pigmented areas. Later on, yellow streaks and spots appear, the secretion becomes more and more opaque, with an increase in the amount of the solid constituents increases in amount, and acquires gradually a homogeneous, yellow appearance.

The early observers frequently attempted to determine some external features which should be characteristic of tubercular sputum, and many hypotheses were built up, only to fall a prey to criticism. In general, when there is a nummular sputum which sinks in water (sputa globosa nummularia, fundum petentia), which has a circular, apparently gnawed out surface, and a thin coating of clear, viscid mucus, it is safe to ascribe it to cavities. Yet just such sputa may originate in bronchiectases. The sputum often contains light red points and filaments of blood; at times it is mingled with pure blood or consists of blood entirely. In other cases the admixture of extravasated blood gives it a dirty brick-red or even rusty color and the appearance of raw meat. The color varies somewhat, also, through the action of chromogenic bacteria. Yellow and red discoloration are produced by B. aureus and squamosus, Sarcina lutea aurantiaca and variegata (Panizza); green discoloration is traceable to Bacillus pyocyaneus (Cornet) and to Bacillus fluorescens (Pansini). Now and again we find stony secretions, which come from the calcareous masses formed by the deposition in smaller caseous foci of the phosphates and carbonates of lime ("Lungensteine"). The taste of the sputum is sweetish, the odor often sweet, nauseous, even intensely fetid.

The amount of sputum varies greatly. Some patients will cough only two or three times a morning, while others will expectorate a pint. Some, again, especially women and children, swallow the sputum, consciously or not. Sputum is scant if the disease tends to spread along the lymph- or blood-channels, while where there is cavity formation sputum is abundant. At times the cavities dry out and the expectoration sinks to a minimum or disappears. Shortly before death, when the patient becomes too weak to expectorate, the sputum apparently diminishes in quantity.

The evacuation of the secretion either is easy or is accomplished only by violent coughing. Especially noteworthy is the dry, short crack during respiration, which has been mentioned by Piorry and emphasized by Dettweiler. This note is perceptible, sometimes at several paces' distance, when the patient is quiet, or even recumbent; it frequently causes him much annoyance, goads him to repeated hacking and coughing, and keeps him from sleep. It is explained as a râle in a cavity in the upper lobes, intensified by resonance, and transmitted by a large bronchus.

Constituents of the Sputum.—The most important and noteworthy constituent is the tubercle bacillus, whose presence is the most valuable factor in diagnosis. It is hardly necessary, at this late date, to discuss in detail the numerous contributions of Balmer and Fräntzel, Guttmann, Ziehl, v. Leyden and Merkel, Lichtheim, and many others. Their conclusions in regard to the presence of tubercle bacilli in sputum are unanimous. The importance of this discovery is due to the fact that the tubercle bacilli are often demonstrable at a time when the physical signs of the disease are still ambiguous. At other times, indeed, the bacilli are absent, either because there is no ulcerating focus, as in miliary tuberculosis, or because the cheesy area is not in communication with a bronchus. In addition to the tubercle bacillus, one finds a variety of other forms, which come in part from the upper respiratory passages and the mouth, and are generally found in the outer layers of the sputum (sarcinæ, etc.); in part from the pulmonary foci and cavities, where they have played the rôle of innocent parasites or of active agents in the disease (see above, Mixed Infection).

The microscopic examination of the sputa reveals, in addition, the epithelium of the various passages,—trachea, bronchi, mouth, and larynx,—squamous and cylindrical in character; furthermore, ciliated cells, leucocytes, cells undergoing granular degeneration, and detritus.

The presence of pigment cells and myelin cells in large number, the so-called alveolar and epithelial cells of the lung, was adduced especially by Buhl as evidence of a desquamative pneumonia, namely, phthisis. By other authors—Bizzozero, Guttmann, and Schmidt—they were found also in fibrous and catarrhal pneumonia, in bronchitis, and lastly in the sputum of healthy individuals over thirty-five. Panizza investigated the sputum of 500 sick and healthy persons, and found in 86 per cent. of the healthy that pigment cells and myelin forms were present, especially where the respiratory surface had been subjected to slight irritation, as, for example, by a warm, smoke-charged atmosphere. "Myelin" is identified by Panizza with a certain form of mucus, which does not dissolve, but swells up in water. This mucus is cast off by the goblet cells lying in the ciliated epithelium upon slight irritation, takes up the pigment granules which lie on the surface, and is carried outward by the ciliary motion as myelin or pigment cells. This does not exclude the fact that the alveolar epithelium may also absorb pigment, and may give rise to the presence of large, pigmented, myelin cells in the sputum.

Especially important in phthisical sputum are the elastic fibers, the only constituents which withstand caseous destruction. V. Sokolowski and Greif found them in about 70 per cent., Dettweiler and Setzer in 90 per cent., of 110 phthisical patients in various stages. There was a tendency to ascribe pathognomonic significance to these fibers, but this is incorrect, since they are found also in other processes associated with destruction of the lung, such as gangrene, abscess, or infarct. Even the macroscopic examination of the sputum, when thinly spread, enables one to detect the elastic fibers in the opaque, dirty gray or reddish-yellow particles, which to the naked eye look like bread-crumbs (Kaatzer). The addition of dilute potassic hydrate or strong acetic acid to the preparation serves to destroy the other structures, and the elastic fibers come out so much the more distinctly.

For the purpose of collecting all the elastic fibers out of the sputum, one adds an equal volume of potassium or sodium hydrate, boils for a few minutes, and then permits it to settle or centrifugalize. In cases of rapid destruction of tissue the elastic fibers are often found in large bundles or fibrous network.

It is easy to confuse these elements with the remnants of food retained in the mouth. From cotton they are to be distinguished by their double contour; from crystals of fatty acids, by the fact that the latter fuse with slight warming, and become changed into fat-globules.

The chemical constitution of phthisical sputum has been worked out by Biermer. He found 88 to 98 per cent. of water, 3 to 11 per cent. organic matter, 0.7 to 0.9 per cent. inorganic matter. Bamberger in chronic tuberculosis found 94.5 per cent. water, 4.7 per cent. organic and 0.8 per cent. inorganic matter. Renk tried to determine whether the amount of albumin lost in the sputum was of consequence to the organism. He calculated that the loss of nitrogenous matter by way of the sputum ran up to 0.75 gm. on the average in twenty-four hours; in other words, amounted to 6 per cent. of the nitrogen excreted by fasting individuals, or 3.8 per cent. of that excreted by the well-nourished. Renk found 94 to 95 per cent. water, 0.76 to 0.95 inorganic matter, including sodium chlorid and phosphates, and 4.13 to 5.36 per cent. organic matter (1.8 to 2.84 per cent. mucin, 1.26 to 2 per cent. extractives, 0.2 to 0.49 per cent. albumin, 0.3 to 0.52 per cent. fat). Of other compounds, tyrosin (v. Leyden and Jaffe), glycogen (Salomon), urea (Fleischer), have occasionally been found. Bokay found the fats of fatty acids to be 9.7 per cent., free fatty acids 0.9 per cent., cholesterin 0.14 per cent., lecithin 1.245 per cent., albuminous matter 5.115 per cent., nuclein 0.489 per cent. Kossel found 0.1 to 0.334 per cent. of nuclein. According to Fr. Müller, the ordinary nummular phthisical sputum contains no bacteria which liquefy gelatin,—*i. e.*, peptonize,—whereas in bronchiectatic sputum these do occur. Escherich separated a digestive ferment from phthisical sputum with alcohol. Fr. Müller, also, was able to show that the glycerin extract of purulent phthisical sputum exercised a digestive action on fibrin and coagulated albumin. If decomposition sets in, or if heat up to 60° C. (140° F.) be applied, and the sputum be then shaken up, it is changed to an absolutely homogeneous, thin, milky fluid (Müller, Kossel). Müller explained this as due to the decomposition of the mucin. The specific gravity of the fluid so obtained fluctuated between 1037.5 and 1006.0; in the mean, 1021.5.

PULMONARY HEMORRHAGE.

Whereas cough and expectoration are constant accompaniments of pulmonary tuberculosis, hemoptysis occurs only in a certain proportion of the cases; in 24 per cent. according to Condie, 70 per cent. according to Williams, 66 per cent. according to Brehmer, in 34.5 per cent. of 403 according to Abraham. Many authors believe it to be more frequent in women—according to Louis, in the proportion of 3 to 2; Abraham, on the other hand, fixed the opposite ratio of 2 to 3. Age is an important factor, inasmuch as previous to puberty, especially before the second dentition, hemoptysis occurs very rarely.

Rilliet and Barthez asserted that they had never seen pulmonary hemorrhage in children under six; such cases have, however, been reported by Henoch, Baginsky, Carrie, Rasmussen, O. Wyss and Hoffnung. Lebert, also, saw a fatal hemorrhage in a child of two.

Most frequently the hemorrhage occurs in the very beginning of the disease. Not rarely it precedes all the other phenomena and overtakes the victim in an apparently flourishing condition. This has led to the widespread but mistaken idea that the hemoptysis is in itself the cause of the subsequent phthisis (Phthisis ab Hämoptoë), an idea which was exploited especially by Morton, and was later taken up and defended by Niemeyer. The theory was that the blood which had been effused into the alveoli dried out and underwent caseous degeneration. This belief may now be considered definitely overthrown. In the first place, the researches of Perl and Lipmann have shown that blood effused into the trachea and bronchi is rapidly absorbed without producing any irritative phenomena. Secondly, the presence of bacilli in the fresh blood of an initial hemoptysis, as demonstrated by Hiller, Germain Sée, Cochez, and Hugueny, proves that the bleeding is not the cause but a symptom of pulmonary tuberculosis, and is the result of a preceding infection of the lungs.

The origin of hemorrhage is easily explained. The living bacillus, derived from a disorganized tubercle, finds its way into a perivascular lymph-channel, deposits itself on the wall of a vessel, and by proliferation invades this wall. Altered in this manner, the vessel loses its power of resistance against the blood-pressure, so that even under normal conditions, but especially if the blood-pressure becomes increased, the diseased vessel bursts and the blood pours out into the lung. This process is, however, exceptional; as a rule, the proteins have already distributed themselves in the vicinity of the tubercle, and have produced an inflammatory reaction on the part of the capillaries and obliteration of the lumen. Hemorrhages of the kind just described, therefore, occur only while the proteins are still scarce; that is to say, at the beginning of the process.

Rindfleisch, Rühle, and Sée assert that the lumen of a terminal artery which has no anastomoses is narrowed by a tubercle; that there is a consequent rise of blood-pressure, especially marked at the constriction; and that in this wise a rupture, a hemorrhage occurs, which is controlled only by the formation of a thrombus. These explanations refer chiefly to hemorrhages which arise in the inception of the disease.

The conditions are often changed after cavity formation has set in. At this stage we frequently find cylindrical aneurysms which course along the wall of the cavity, or protrude into its lumen, and also vessels which traverse it. Here, too, rupture may occur under conditions of increased blood-pressure, especially if the vessel-wall is implicated in the disease and lacks the support of the surrounding connective tissue. The hemorrhage in this case is generally much more serious, and, owing to the difficulty of adequate thrombosis, far more uncontrollable. Indeed, there is danger of exsanguination, which is on the whole not frequent, yet does now and then occur.

At times hemorrhages are due to over-congestion of the lung. Finally, there is the possibility, of far less importance, that blood-corpuscles may wander by diapedesis into the tissue around the blood-vessels, and may become mingled with the sputum as spots or streaks of blood.

In some cases there is only a slight attack of hemoptysis, at the onset of the disease; in others it recurs at long intervals; now and again, however, it continually repeats itself, perhaps as the expression of a minor degree of hemophilia, so that the phthisis assumes a peculiar character (hemoptoic phthisis).

The amount of blood lost varies greatly. The hemorrhage may be limited to a few red spots or streaks in the sputum, often overlooked, which again disappear; or the sputa may become rose-colored; or, again, if the blood has been extravasated for some time, dark coagula are formed which become intimately mingled with the mucus and sputum, and give a red, reddish-yellow, or reddish-brown color.

Often a hemorrhage occurs without the slightest warning. The patient wakes, for example, toward morning, has a slight irritation in his throat, coughs, feels "something warm" under the sternum, has a sweet taste in his mouth, and, to his terror, discovers the bright red color—sees, in a word, that it is blood. He has to expectorate twice or three times again, and for the time the attack is over. Especially in hemorrhages in the initial stage, the loss of blood often does not exceed two or three teaspoonfuls. In other cases the amount may reach to 100, 200, even 1000 cc. and more; the blood flows without cessation, even gushes out of the mouth or nose (blood-gush), and may threaten life itself by suffocation and anemia. In many hemorrhages the crepitation and gurgling in the chest produced by the effusion of blood into the bronchi are perceptible to those around. Even after the hemorrhage is over the sputum retains a bloody discoloration which in the next few days becomes darker, and finally disappears. Frequently the hemorrhage is repeated once or twice during the next eight days, and then disappears for a long period or for good.

Larger hemorrhages are often heralded by bloody streaks in the sputum, also by traces of blood in the nasal secretion, by a feeling of oppression on the chest, by an irritation of the throat often of several days' duration; or they come apparently out of a clear sky, the patient being in prime condition or on the road to recovery. In some cases they result after severe exertion, a cold bath, or a forced march, especially in the heat of the sun. I remember, for example, the case of a patient who hurried down the steps in order to give a letter for his bride to a passing mail-wagon; at the foot of the stairs he was stricken by a hemorrhage, which shortly proved fatal. Pronounced mental excitement, depressions, or fits of crying may likewise give occasion to hemorrhage. We find an increased frequency under the influence of atmospheric conditions, although we have not as yet been able to identify the actual causative factor. Rohden attributes these hemorrhages to sudden changes, especially to a rapid rise in humidity, with the explanation that the hindrance to the excretion of water through skin and lungs leads to a corresponding plethora, to an increase in the pressure in the pulmonary circulation, and so to conditions favoring hemorrhage. Blumenfeld and Goldschmidt have also made an effort to explain these conditions, but have not reached any positive conclusions.

It still remains for us to consider the question how far pulmonary hemorrhages are of a tubercular nature, and how far they may be simulated by other forms of hemorrhage. All in all, one does not err in considering actual pulmonary hemorrhages to be of tubercular nature, although hemorrhages do occur in certain other diseases, in hemophilia, pneumonia (abscesses and gangrene), and aneurysms of the aorta. Diseases of the heart, especially mitral stenosis, and diseases of the tricuspid are important causes of bloody infarcts; but in such cases a careful examination reveals the etiology.

Especially worthy of mention among the non-tubercular forms of hemorrhage are such as occur in women, partially or entirely replacing the menstrual flow (vicarious hemoptysis). It does undoubtedly occur, though on the whole but rarely. Several years ago I observed such a case, in which for a number of months the menses were absent, and were replaced during the same period by a pulmonary hemorrhage of from two to three teaspoonfuls. The patient showed absolutely no signs of pulmonary disease either at the time or subsequently, for she was given a most careful examination and was kept under observation for a long period. Such vicarious hemorrhages have frequently been described in phthisical patients. Kober, in Beuthen, observed the case of a phthisical young woman who repeatedly had hemorrhage from the lungs at the time of the menses, the latter being at first reduced in amount and finally completely lost. The absence of a customary hemorrhoidal hemorrhage has been made responsible for certain cases of bloody expectoration. Although there is, indeed, little doubt of the possibility of such an origin, one should studiously avoid a too liberal use of this conception of vicarious hemorrhage.

Periodic attacks of hemoptysis as an expression of malaria have been described by Silberschmidt, and Löwenthal, and are to be considered as one of the forms of masked intermittent. Especially worthy of note are the pulmonary hemorrhages consequent upon vasomotor disturbances in hysteria. This leads not to severe bleeding, but to a reddish discoloration of the sputum, lasting often over long periods.

In other cases one must be careful to exclude hemorrhages from the mouth, the gums, and the throat. Especially confusing is the blood which runs from the nose and collects in the nasopharynx during the night; it gives rise to nocturnal hemorrhages which leave red spots on the pillow and cause the patient undue anxiety.

Further, one must weigh the question, especially in rather large hemorrhages, whether the blood does not come from the stomach, and does not express a hematemesis. In gastric hemorrhage the blood is thrown up more than once, has generally a darker or even blackish color, and frequently gives an acid reaction owing to the admixture of gastric juice; at the same time we miss the cough as well as the râles, which are produced by the retention of some of the blood in the bronchi.

DYSPNEA.

Dyspnea is a symptom which varies extremely both in occurrence and in intensity. What are the etiological factors which underlie it? It depends, in part, upon a limitation of the respiratory area, in part upon nervous influences; emanating from the vagus and its terminations, it is often due to an emphysema of vicarious nature or to fever. As regards the diminution of the respiratory surface, it is surprising to see how the organism will tolerate pronounced disturbances of this nature without any real complaint. Time and again we find that a slowly developing pleurisy produces either slight disturbances of respiration or none at all, and this even though half the chest be filled with fluid and half the lung thrown out of action. A pneumothorax, on the other hand, by the very suddenness of its occurrence may produce the most urgent symptoms of asphyxia. Thus, we find that in a gradually developing chronic phthisis, extensive changes, cavity formation, and infiltration do not seriously embarrass the breathing of the patient. It is absolutely incredible with how little of the lung life may be maintained, and what extensive areas may be destroyed and thrown out of function. I have in mind the case of a patient, one of the first of those treated with tuberculin, in whom the autopsy a year later showed that more than two-thirds of the lung had been transformed into indurated and cicatricial tissue, while death came only as the result of an influenza compromising the small remainder of the lung. The degree of dyspnea is, therefore, no criterion of the extent of the disease, but depends essentially on the rapidity with which larger or smaller areas of the pulmonary surface are excluded from service.

In addition to this mechanical cause, we have also mentioned the irritation of the vagus endings by the tubercles, which especially affects the frequency of respiration. This factor likewise gains especial prominence when large areas are simultaneously irritated, as in acute miliary tuberculosis of the lungs, in which an asphyctic condition may occasionally arise, whereas chronic attacks do not seriously embarrass respiration. The pressure of enlarged, cheesy bronchial glands upon the vagus may also give rise to severe dyspnea; an example of this is to be found in the attacks of dyspnea with severe coughing spells in children.

It happens, indeed, that phthisical patients get rapid breathing, with a certain feeling of pressure on the chest from other causes, even at the very beginning of their sickness, so that after the exclusion of other possible etiological factors—bronchi, heart, and vessels—the presence of phthisis may be strongly suspected. But in general the dyspnea develops gradually, and the invalid, if he does not exert himself, is scarcely aware of it. Many patients even boast of their ease in breathing and of their "wind," and disregard the over-anxious warnings of their doctor. Only after considerable bodily exertion, climbing stairs or mountains, or after coughing, singing, or prolonged conversation, does the respiration increase in frequency and the patient "lose wind." After meals, when the stomach is disturbed, there is a sense of compression in the chest, which is in part due to a slight rise of temperature. But as soon as the patient takes a rest, breathing again becomes free and untrammeled, and a certain degree of air-hunger is betrayed only by an occasional deeper gasp. The patient ordinarily compensates diminished depth of respiration by an increase of frequency.

The phenomena of dyspnea are often hardly noticeable even in the advanced stages, especially if the patient observes greater quiet for other reasons. Dyspnea is increased if large areas of lung be all at once thrown out of function by the aspiration of secretion; if the gaseous interchange be interfered with by hyperemia, by acute catarrh, hemorrhage, edema, bronchopneumonia, pleurisy, or emphysema; also in all or in most cases associated with fever, which of itself diminishes the depth while it increases the frequency of respiration. Now and then, especially toward the close of the disease, the dyspnea is of a high grade. It comes on if the patient walks about the room, if he removes his clothes, if he turns in bed, and with the slightest exertion leads to actual suffocation (orthopnea); with desperate gasps, the sufferer painfully struggles for air.

Dyspnea is to a very great extent manifestly dependent upon the nervous condition of the patient, inasmuch as irritable individuals, women and children, frequently suffer more than others from tachypnea; chlorotics, likewise, often show marked disturbances of respiration from the very beginning. Now and again in phthisis there are real asthmatic attacks; the patient awakes at night or toward morning, cannot maintain his recumbent position, jumps out of bed to the window, and struggles for air. Such a case I had under treatment several years ago. The attacks recurred frequently, lasted several minutes, and were succeeded by quiet, normal breathing, but all the other characteristics of a bronchial asthma were lacking. These asthmatic phenomena may so dominate the picture that the patients describe the entire symptom-complex as asthma.

HOARSENESS.

Excluding for the time tuberculous laryngitis proper, which of course can elicit pronounced disturbances, we may state it to be the rule that after a certain duration of the disease the voice increases in intensity, and that prolonged talking is followed by a feeling of exhaustion which may be referred as far as to the apex of the diseased lung. This is to be interpreted as an expression of the weakness of the respiratory blast, of the respiratory musculature, and of the body as a whole. Similar conditions are found to obtain in cholera, and even in severe diarrhea. As the disease progresses, the voice loses in clearness, becomes slightly muffled, dull, and finally hoarse and inflexible; it traverses every grade of dysphonia and aphonia, and sinks finally to a harsh and tuneless murmur. At first the hoarseness is only fleeting, and comes from excitement or changes of temperature; it passes quickly, but frequently recurs, and eventually becomes continuous. Such is the general course, but variations from it in either direction are not infrequent. Certain patients retain a clear and resonant voice up to the very time of death. They are able to sing, to hold prolonged discourses, to shout, and to command; the strength of their voices hides the condition of their lungs and deludes them into a false sense of security. The voice may regain its original power even just before death. I had a woman with phthisis who for two years spoke only in a weak, soft voice, often reduced to a whisper. A few hours before her death, in a condition of mental aberration, she made a long speech, which was delivered in a beautiful, bell-like voice, audible across two rooms. On the other hand, in some patients hoarseness develops early, and so dominates the picture that all other symptoms take the background. In such cases there is often a continual tickling and irritation in the throat, and a dry cough, with scanty, clear, mucoid sputum occasionally mingled with pus or streaked with blood from the coughing effort. These throat symptoms are intensified by cold air, stimulating drinks, wine, so that they become at times unendurable; they thus acquire a paroxysmal character.

Now and again there occurs a hoarseness, perhaps not very marked, but extremely obstinate—a muffled voice—which appears at a stage previous to any other pulmonary symptoms. This prodromal hoarseness, which has been especially emphasized by Schäffer, Libermann, and Martel, may first awaken the anxiety of the patient and his friends and, as a diagnostic sign, is worthy of close observation. The cause of this hoarseness is not necessarily to be sought in tubercular infection, a secondary involvement of the laryngeal mucosa, although this is always first to be considered. It is rather to be attributed in part to the other non-tubercular changes, which often accompany phthisis, and in part to the paralytic processes. Thus we find that congestion, acute or chronic catarrh, are produced by violent coughing, or by the chemical action of the sputum, or by any of those conditions which in health exert a similar action. The vocal cords are reddened and swollen, and a tough secretion covers them or stretches across from one to the other in long adherent threads, which interferes with their freedom. There may be superficial erosions and losses of epithelium, which are not necessarily tubercular in nature and of which we have already spoken (pages 168, 173). A further possible cause of the hoarseness is syphilitic laryngitis, either alone or combined with tuberculous disease (page 174), or the hoarseness may depend upon a single or double paralysis of the inferior laryngeal or recurrent nerve, which by its long course is especially exposed to external influences. The lymph-glands lying between the trachea and esophagus and the bronchial glands are especially prone to exert pressure on the recurrens when they become swollen. The tubercular tumefaction and swelling of these nodes is often an early phenomenon, and may even precede the pulmonary infection. It is, therefore, easily comprehensible that a vocal paralysis and hoarseness should form the first manifestations of a tuberculosis of the lungs, even though it involves, as is frequently the case, the same side of the larynx. Further, the right recurrens is often injured by pleuritic thickenings and infiltrations at the apex; while the left suffers through large, acute pleuritic exudates and pleuritic thickenings at the hilus, and also through pericardial exudations. At times it is not a matter of pressure atrophy, but of inflammatory processes in the nerves.

In a case of phthisis which was daily inspected on account of tracheal disease, Landgraf found a left-sided posticus paralysis, which in forty-eight hours had been changed to a left recurrens paralysis. The patient died, and at autopsy it was found that the fibers of both posterior cricoarytenoids had undergone marked fatty degeneration, and that the left was paler than the right. By "teasing" apart the left recurrens (Siemerling), it was found that hardly any normal nerve-fibers were left, that most of them either possessed no medullary sheath or that it had become fragmented and dissociated, and that the axis-cylinders were no more to be made out. There was a small lymph-node, barely enlarged and not at all caseous, which was found resting upon the recurrens just under the arch of the aorta. Landgraf concluded that the degeneration of the nerve had not resulted from pressure, but that there had been a primary inflammation of the neurilemma which had eventually involved the interfibrillar connective tissue.

E. Fränkel has described especially in the laryngeal musculature, but also in the other muscles in phthisis, a number of histological changes of a degenerative character, including fatty degeneration of the muscles and interstitial hyperplasia (see Pathological Anatomy, page 358), to which he is inclined to attribute the hoarseness.

DYSPHAGIA.

True dysphagia occurs, as a rule, only after the disease has localized itself in the pharynx and the larynx. Nevertheless difficulty in swallowing forms one of the more frequent complaints of the tubercular. The patient eats and drinks with a relative degree of comfort, when all at once a particle of food may enter the pharynx and inaugurate an attack of coughing of a very violent character, paroxysmal, and ending perhaps with vomiting. This occurrence is so frequent that the patient comes to avoid his meals and approaches them only with a pitiable dread. Or, while he is lying quietly asleep, a drop of saliva falls down the larynx; he awakes with an explosive cough, with an unendurable tickling and irritation in the throat; the cough may last a quarter of an hour, makes the patient dyspneic, exhausts him, and renders sleep for a long time afterward impossible. Also in dyspeptic eructations, especially of spicy articles of food, a least trace may enter the larynx, and the same process ensues.

Apparently this frequent trouble in swallowing depends upon a paralysis of the depressors of the larynx, the thyro-aryepiglottic muscles. This, again, is due to paralysis of the superior laryngeal nerve, a branch of the vagus, of which the external division supplies the cricothyroids (tensors of the cords) and thyro-aryepiglottic muscles (depressors of the epiglottis in swallowing), while the internal division gives sensation to the mucous membrane of the larynx from the pharynx down to the free border of the cords (Luschka).

PAIN.

Still another though inconstant symptom of pulmonary tuberculosis is pain, especially over the site of disease. Many cases run the entire course of the disease without ever complaining of pain, whereas in others, again, it constitutes one of the chief complaints. The pain tends especially to be localized either at the apices or in the anterior chest-wall below the clavicle to the third rib, in the intercostal spaces; or in the back, below the scapulæ and between them; and frequently in the neighborhood of the nipple. As a rule, the diseased side is preëminently or exclusively involved, while the unaffected side is only exceptionally the seat of pain. Now and then the pain is situated at the base of the thorax, laterally, at the points of attachment of the diaphragm and especially of the muscles.

The pains are often slight, especially in the earlier stages, and are discovered only by inquiry. They are rarely constant, being generally fleeting and intermittent; they are often intensified by deep respiration, coughing, sneezing, laughing and crying. In part, they depend on hyperesthesia, which becomes evident upon percussion, pressure, or slight touch, and in the recumbent position. This hyperesthesia involves chiefly the sternum and the third and fourth dorsal vertebræ. The pain is most often characterized as "sharp"; in other cases, either spontaneously or after coughing or prolonged talking, there comes a feeling of "tiredness" in the corresponding areas of the chest, a feeling of "emptiness" or "soreness" in the chest, midway between the back and the sternum. As the pains vary in position, they are often regarded as rheumatic.

The causes of the pain are various. In particular, there are the pleuritic changes, *traction* on the almost never failing adhesions. The pulmonary parenchyma as such cannot originate pain, so that the largest cavities form very rapidly without any sensory disturbance, and even pleuritic processes, which in phthisis are hardly ever lacking, produce pain only when rather acute in nature, whereas the chronic changes develop insidiously and without signs. Now and again a slight pleuritic rub betrays a circumscribed area of inflammation. Sometimes this is an indication of pulmonary congestion, and may precede hemoptysis by several days. I had a patient in my care who could predict a hemorrhage three or four days in advance, simply from the onset and the increase of her pains.

The pains at the muscular attachments are often explicable as a functional exhaustion due to the severe respiratory effort of cough or of dyspnea, and may be compared to riders' or gymnasts' cramps. It is possible, too, that disorders of nutrition in the muscle may contribute to this symptom.

Neuralgias occur at times in the intercostal nerves, the trigeminus, and the sciatic. Hérard, Cornil and Hanot found a very severe case of sciatica to be complicated by a pulmonary tuberculosis, and at autopsy, in addition to other changes, a tubercular meningitis on the side of the neuralgia was discovered. (See also Nerve Symptoms.)

Neuritis must be considered an etiological factor in some cases.

Under the name of "melalgia," Beau has described certain very severe pains which occur in advanced phthisis. They are elicited by pressure over the knee, sometimes involve the entire limb, are continuous, worse at night, and reduce the patient seriously.

Especially severe are the pains in cases of pronounced dry pleurisy, and most severe of all in pneumothorax. In the last-named condition they come like an explosion, involve a wide area, interfere with breathing and lying down, and produce severe dyspnea.

In conclusion, we may say that pain, even at the onset of the disease, being an indication of superficial, subpleural infiltration, is a forerunner of other symptoms, and as such is of diagnostic value. Such pain is, as a rule, not severe. During the last months of life the pain may be enormously increased and the patient's condition become really pitiable.

More rarely we find anesthesias and analgesias, or paresthesia in hands and feet, the sensation of "being asleep."

The anesthesia of the larynx, as a cause of faulty deglutition, and also hyperesthesia, have already been considered.

CONSTITUTIONAL SYMPTOMS.

Every tuberculous infection is associated with the manufacture of metabolic products; furthermore, since the tubercle bacilli have frequently only a brief existence and are then destroyed, there are also the products of disorganization. These two classes of compounds, the ptomains and the proteins, are diffusible, and invade the tissue surrounding the tubercle. They produce, by their relative concentration, a series of reactive phenomena in the immediate environment; lead to exudation and to a certain extent produce stasis and obliteration of the vessels. On the other hand, they are also absorbed by the tissue-fluids, are carried off, and so enter the blood-stream. Outside of the tuberculous focus one may also, therefore, describe a circumferential poison-zone (Giftzone), which is often only faintly differentiated, and shades off into the healthy tissue beyond. The easier it is to bridge the tissue-spaces, the more active the metabolic process, so much less successful is the attempt to concentrate bacterial poison in the immediate periphery of the focus, and in proportion to the failure to accomplish this is the rate of their absorption by the lymph and the blood-stream.

Where the focus is small, the formation and the absorption of the poisons is limited in amount, often minimal; consequently the changes undergone by the blood and the body-fluids in general are correspondingly slight. The larger the focus, the greater the amount of the poison produced, and the more extensive the area of absorption, the more, *ceteris paribus*, is absorption favored and the greater are the alterations produced in the tissue-fluids. Therefore the degree in which changes in the tissue-juices and in which constitutional symptoms manifest themselves is dependent primarily on the size of the tubercular focus, on the area of the peripheral absorptive surface, and on the absorptive capacity of the circulatory channels. With regard to the last point, there is considerable variability at different ages; the young absorb much more rapidly and freely than the mature or the aged. This furnishes an explanation of the fact that children, as compared with adults, present a much stormier reaction, a much more violent type of constitutional symptoms, not only in tuberculosis, but in the infections of all other diseases. This assertion is only an hypothesis, which has, however, at least as much justification as the other causes to which this age variability is attributed.

Hand-in-hand with this rapid absorption goes a correspondingly rapid freeing of the environment of the tubercular focus from the poisonous material. Since, however, the reactive inflammation which these compounds set up affords a barrier—uncertain, indeed, but still not to be despised—against the incursions of the tubercle bacilli, it follows that in youth, or in an analogous constitutional condition, the tubercular process spreads much more rapidly than in later life; for in later life the poisons remain for a time in a certain degree of concentration and set up indurative processes. The barrier thus formed is not, as has been said, absolutely impregnable, for in spite of it an occasional living bacillus is borne across it at one point or another and inaugurates a fresh focus. But by the constant repetition of this process it makes an essential difference in the course of the disease whether the bacilli are able to force a narrow passage here and there or whether the entire circumference of the focus is open to them.

The intensity of the symptoms is essentially an expression of the degree of concentration of the bacterial poisons in the blood, and this, again, depends on two factors: not only the amount of the poison absorbed, but also the amount of blood in the organism. This fact has come to be neglected, because of an erroneous comparison with other infectious diseases. If, for example, a small and a large animal of the same species are inoculated with anthrax, the latter generally perishes somewhat later. The difference of time is, however, not at all considerable, for the anthrax bacillus proliferates in the blood itself, and reaches the acme of the process practically simultaneously in both animals. Even in typhoid or cholera the course is not to any extent accelerated in a smaller animal; for the more extended the intestinal tract, the richer is the soil for growth; thus the greater quantity of blood is offset by an increased production of poisons, and the relation between the two—the poisons, on the one hand, and the tissue-juices and blood, on the other—maintains a fairly constant ratio.

In tuberculosis matters are radically altered, for this is a disease which remains strictly localized. Let us assume, for example, that a guinea-pig weighing 300 gm., a child of 6 kg., or twenty times the weight of the guinea-pig, and an adult of 60 kg., or 200 times that weight, simultaneously inspire a tubercle bacillus or a colony of bacilli. Assuming an equal rate of growth or an equal proliferation capacity in all, a focus of the size of a pea is formed in the lung inside of eight to ten weeks. Such a focus constitutes a considerable portion of the entire lung of the guinea-pig, a rather small fraction of that of the twenty times larger lung of the child, and in the lung of the adult becomes a negligible factor. With progressive growth dyspnea becomes very evident in the guinea-pig within a few weeks; in the child the first symptoms, perhaps, become manifest; in the adult no external signs of the disease are to be made out; yet in all three organisms the foci have almost equal dimensions. The diversities in these reactions are not lightly to be explained away as idiosyncratic differences, inasmuch as the conditions really indicate a far simpler explanation. If we hold to the above examples, foci of equal size and age produce almost equal quantities of poison, and if we assume an equal capacity for absorption, although in fact it seems to be more lively in the child than in the adult, and in the guinea-pig than in the child, then equal quantities of poison are distributed in one case in about 25 gm. of blood; in the second, the child, in 500 gm.; and in the adult, in 5000 gm. of blood. Corresponding to these different degrees of concentration the guinea-pig may show almost fatal symptoms, the child, at the same time, only slight symptoms, and the adult no symptoms at all, either subjective or objective.

BLOOD.

In the blood one might expect the first changes in constitution, the first evidence of the action of the proteins, since this is the first tissue invaded by the poisons absorbed from the tubercular foci. As a fact, the changes in the blood express themselves usually very early in a series of symptoms which externally mimic the picture of anemia—facial pallor, ashy discoloration of the skin, weakness, and emaciation. Strikingly enough, however, the chemical and morphological composition of the blood does not evince a correspondingly intense alteration, at least in so far as our present methods of investigation afford us an insight into them. It is not to be denied that now and again most severe anemias originate from tubercular infections; v. Limbeck observed such a case, in which the number of red cells fell to 730,000, the number of white to 4300, and the hemoglobin, measured by Fleischl's apparatus, reached only 25 per cent. of the normal. Such figures are, however, very rare, and there are cases in plenty of the opposite description, in which the almost normal quantity of red cells and hemoglobin stands in no ratio to the visible disturbance of the economy of the blood and to the extreme cachexia of the patient.

In most cases of tuberculosis we have to deal with a decrease in the number of red cells and a diminution in the hemoglobin content, as is evident from the researches of Malassez, Quinquaud, Lacker, Bierfreund and Fenoglio. Normal blood contains to the cubic millimeter 5,000,000 red cells in men, 4,500,000 in women; the white cells are in a ratio of 1 to from 500 to 800,—that is to say, 6000 to 10,000 in men, 6000 to 9000 in women; the hemoglobin content of 1 gm. of blood is 0.1377 in men, 0.1259 in women. Malassez found a diminution of the red cells in severe phthisis to 2,560,000 in men, and to 930,000 in women, for each cubic millimeter. Sörensen found an average of 4.35 millions in 11 far advanced cases. In 14 cases, investigated by Laache, in which there was in part cavity formation, the counts ranged from 5,220,000 to 2,400,000 per cc. Dehio reached similar results. Further investigations have been published by Häberlin, Neubert, Reinert, Grawitz, and Strauer. Neubert found a not very severe hemoglinemia of 85 per cent. of the normal in men, of 73 per cent. in women.

If one accepts Grawitz's subdivision of the tuberculous into groups, the first stage, the so-called "apical catarrh," is associated with distinct signs of anemia. The count of red blood-cells, according to Grawitz and Strauer, is reduced, that of the white cells variable, and the solid residue of blood and serum, as also the specific gravity of the blood, is diminished. In strong individuals without pallor normal conditions are also found. According to v. Limbeck and Dehio, the number of erythrocytes is often normal, the chromatophilic substance, however, reduced. Such cases, which are especially frequent in women, give the clinical picture of pseudochlorosis, and are not to be distinguished, as far as regards the blood-count, from true chlorosis. The leucocyte count, according to Neubert and v. Limbeck, not only in the first stage of a chronic uncomplicated pulmonary tuberculosis, but also in all cases of simple tubercular infection, remains normal.

In the second group of cases, comprising the chronic phthises without especial complications, with cavity formation and with no or only a slight degree of fever, the blood rises slightly or not at all from the normal, although there is marked pallor of the skin. Ordinarily there is only a slight increase in the leucocytes, which may count up to from 12,000 to 15,000.

In the third group, with markedly remittent or intermittent fever, especially of the hectic type, Grawitz found that the erythrocytes and the hemoglobin content were markedly diminished, the leucocytes often increased, the solid residue of blood and serum reduced, and the specific gravity correspondingly lowered. These conditions are found to increase progressively with the duration of the fever.

According to v. Limbeck, in cases which are associated with a high and hectic fever, and in which there is a certainty of a secondary septic infection, leucocytosis is rarely missing, whereas it is never present when the fever is to be traced to an acute miliary or submiliary exacerbation of the disease. This fact he considers of importance for the differential diagnosis. Leucocytosis is mostly slight in the chronic sepsis of phthisis, is often marked in the infiltrating form, the so-called caseous pneumonia, and is absent in miliary tuberculosis of the lungs, so that, according to v. Limbeck's researches, in most cases of febrile tuberculosis leucocytosis is an indicator of mixed infection.

It is a striking phenomenon that the initial oligocythemia is replaced, as the disease progresses, by normal conditions, and only returns at the end of the process. Dehio attributes this to a concentration of the blood, through loss of water, especially by profuse sweating, and in many cases by diarrhea. Grawitz, in addition, emphasizes the absorption of certain extractives of tubercular areas discovered by him, which tend simultaneously to stimulate the lymph and to concentrate the blood. v. Limbeck, in addition to the other causes, attributes it largely to a general drying out of the tissues as seen especially in old people, with harsh, dried, wrinkled skin, and deficient sweating. Thus the condition is essentially one of oligemia vera; at all events, an increase of hemogenesis in progressive pulmonary phthisis is not to be considered.

Of other changes in the blood, we may mention the presence of cellulose, demonstrated by E. Freund and Nishimura, an increase in the calcium phosphate (Bequerel and Rodier), and an increase of fibrin, independently of the terminal stages (Walske).

The injection of tuberculin, which to a certain extent is analogous to the direct absorption of the metabolic products of the tubercle bacilli, produces an acute, more or less marked, fleeting leucocytosis and an increase of eosinophiles (Bischoff, Rille, Botkin).

Tubercle bacilli are ordinarily not to be found in the blood, as has already been stated. The edema, due in part to the terminal hydremia, will be described among the skin symptoms. We must also mention the arterial emboli, which are derived from clots in the pulmonary veins; occasionally they implicate the brain and may at times prove fatal.

FEVER.

Closely connected with the absorption of poisons by the blood is the appearance of fever, which outdoes all the other symptoms of phthisis in importance. Exceptionally chronic cases occur, especially in the fibrous form, which run their course without any notable degree of fever, even to a fatal termination. As a rule, however, the course of the disease, and at times even the earlier stage, is associated with a valuable degree of fever, which may continue till the end or may be interrupted by fairly long afebrile intervals. Bilhaut and Eskridge assert that tubercle formation always sets up a rise of temperature. This is, however, very difficult to prove, as in very few cases is the normal temperature of the individual known, and a minimal rise of 0.1° or 0.2° C., especially in those with low temperature, evades proper interpretation.

In phthisis the fever follows no definite type, as in other infectious diseases, but is characterized by irregular variations and changes of character corresponding to the interrupted progression of the disease frequently seen in such invalids. The following classifications of the fever have been proposed: fever with or without chills (Brehmer); fever of the onset, of the course, and of suppuration (Driver); fever of the tubercle-formation, of inflammation, of ulceration, of absorption (Jaccoud, Szekely); fever of continuous type (inflammatory), of intermittent type (hectic), and absorption fever (de Renzi). In reality, none of these classifications is satisfactory, for, even though the general etiology of fever in phthisis is known to us, the effect of the single contributing factors is still too vague to afford a basis of classification for the various types of fever.

Causes.—The tubercle bacillus with the products of its metabolism and decay is without a doubt capable of giving rise to fever. The fever of miliary tuberculosis cannot, indeed, be cited in proof of this theory, since even in the miliary distribution of tubercles there is often a mixture with other bacteria, as is evident from the researches of Kossel, the author, and others. But the febrile reaction following injections of tuberculin makes it sufficiently obvious that the absorption of the tubercle-poisons into the blood and lymph-channels produces a powerful effect upon temperature. We must also admit the febrile action of the products of the pyogenic and other bacteria (streptococci, staphylococci, pyocyaneus, tetragonus), which secondarily infect the cavities, in addition to the harmless parasitic forms (see chapter on "Mixed Infection"). I need only to mention the suppurative fever of surgeons, and the associated hectic. In suppurative fever, in sepsis, there are, ordinarily, marked rises of temperature, inaugurated by a chill, and sharp remissions with profuse sweating. It is, therefore, apparently justifiable to regard a similar fever curve in phthisis as the expression of a secondary or mixed infection. A detailed explanation, however, would demand more complete clinical and experimental researches than are as yet forthcoming. If, through the aspiration of sputum, fresh areas become involved in the disease, pneumonic foci are formed as a result of the irritative action either of the tubercle bacilli and their proteins or of the secondary bacteria; absorption of the poisons from such areas is favored by the fact that they occupy hitherto healthy tissues with patent lymph-channels. An increased and more obstinate fever corresponds to this heightened absorption; the continuous form of fever is ordinarily ascribed to inflammatory processes of this nature.

Height and Course of Fever.—The height and course of the fever I believe to depend, in full accord with de Renzi, in very great degree upon the idiosyncrasies of patients. Even men in health react most diversely to febrile agents. There are torpid individuals, who pass through typhoid or pneumonia without any notable degree of fever (ambulatory cases). On the other hand, there are responsive constitutions in whom the slightest angina produces high fever; now and again one meets with cases in which even marked exertion raises the temperature. These facts may be compared with the idiosyncrasy which certain individuals have for some of the drugs; thus, opium quiets one person, and causes, even in the smallest doses, an extremely restless condition in another, as I recently had occasion to see in a woman under my care.

In some individuals the heat-regulating center is apparently extremely "sensitive." I would recall to the reader the febrile irritability of convalescence from severe diseases, and the fever of hysteria. Phthisical patients, in whom at times the entire nervous system is affected and becomes extremely irritable, would seem to contribute a large contingent to the above category of cases, especially when a prolonged course of fever has heightened the sensitiveness of the heat center. Frequent measurements show that in them even slight physical or mental exertion—for example, a short promenade, the expectation of a visit, long, exciting conversations, piano- or card-playing—produces a rise of several tenths above the norm of the preceding day. Not infrequently the physician is able to announce to the patient some such disturbance, as, for example, the reception of an exciting letter from home, forming his opinion simply from the rise of temperature.

In phthisis, as in anemia, there is often a rise of temperature after meals, especially if heavy, which possibly results from the absorption of nourishment (the "digestive fever" of de Renzi and others). The temperature also depends upon complications, especially secondary infections (*q. v.*). Rises of temperature result from an accompanying pleurisy, pneumonia, peritonitis, or meningitis, whereas profuse hemorrhages and pneumothorax bring about a fall or even a collapse.

From the multiplicity of causes and the variability of the heat center arises the fact that fever is so extraordinarily variable and irregular.

Fever-types.—Notwithstanding the difficulty of an etiological diagnosis of the various forms of tubercular fever, practical considerations, if nothing else, urge us to differentiate certain types. One must, however, keep in mind that the disease itself often varies widely from the schema. We distinguish:

1. A fever which only at certain hours, especially in the afternoon, attains a slight elevation, at most 38° C. (100.4° F.), while the temperature remains normal for the rest of the time—*febricula intermittens*. Ordinarily it commences very insidiously, and, unless regular and frequent tests are made, is apt for a long time to escape detection. During the exacerbation subjective symptoms are either absent or slight. There may be a slight, indefinable malaise; a sensation of warmth in the palms; flushing of the face, especially in circumscribed areas on the cheeks, often more pronounced on the diseased than the healthy side, spots which by the laity are called "churchyard vases"; hot tongue and lips; slightly accelerated breathing; cough, as we find it a few hours after tuberculin injections, a slight chilliness with the onset, sometimes not inconsiderable sweats with the decline; a sleep which is not as quiet and refreshing as it had been. Especially noticeable is the fact that the pulse of the patient during the febrile

period is unusually rapid (90 and over), more rapid, at any rate, than the corresponding temperature requires.

2. Fever which reaches a height of 38° C. (100.4° F.) to 39° C. (102.2° F.), but either returns to normal—*febris intermittens*—or at least shows a fall of more than 1° C.—*febris remittens.* The subjective malaise, the chills and sweats, are more pronounced in this form than in the preceding.

3. Fever rising above 39° C. (102.2° F.), either returning to normal—*perfebris intermittens*—or at least showing a decline over 1° C.—*perfebris remittens.* At times there are actual paroxysms, and in one case, a female patient, I observed a maximum of 42° C. (107.6° F.) for several days. Variations of 4° C. (6.6° F.) and more within several hours are by no means rare. For the most part, this type occurs in the very early stages.

4. Fever of considerable height, which shows remissions below the normal, even to collapse temperatures—hypo-hyperpyrexia. These subnormal temperatures occur toward the close of the disease, indicate a far advanced loss of strength, and are therefore feared as a sign of impending dissolution. With these depressions of temperature, often to 35° C. (95° F.) and below, the patient frequently feels much more miserable than in the paroxysms of the highest fever.

5. Fever of considerable height, mostly above 39° C. (102.2° F.), which shows a daily variation of less than 1° C.—*febris* and *perfebris continua.* Even the morning temperature borders on 39° C. (102.2° F.); the evening rise often exceeds 40° C. (104° F.). This type, as a rule, accompanies the florid form of the disease. The longer such a fever lasts, the less pronounced the morning remissions, and the more severe the chills and sweats, so much the less hope is there of a temporary arrest of the process.

6. The *typus inversus.* This name is given to any of the foregoing types if, instead of the ordinary evening exacerbation and morning remission, the rise occurs in the morning or forenoon and the temperature falls toward night. This form of fever is, on the whole, very rare, and lasts only a short time, passing over into the normal type. It occurs, according to Brunniche, if miliary tuberculosis is added, and especially in the diseases of childhood (Herz). At times this type is artificially produced by the administration of antipyretics, by which the day temperature is somewhat reduced, only to shoot up the more at night.

A fever which is associated with chills and sweats, especially if maximum and minimum lie far apart (steep curves), is ordinarily characterized as hectic or absorption fever; the scope of this conception, however, varies enormously with different authors.

For the rest, the fever may occur at any hour of the day or night. Noteworthy variations of the fever are that it may occasionally show two or even three exacerbations, and that it often differs for successive days from the preceding type, only to return on the second or third day to a similar course.

The sweats, which will be further considered in a special subdivision, and the night-sweats in particular, are not conditioned by the fever alone, although they are frequently to be connected with it. They are not exclusively associated with any of the preceding types, but may accompany any of them. Further, they are in no fixed relation to the height of the fever, and even with the febricula may now and then be very profuse. On the whole, however, their severity increases with the interval between the maximum and minimum of the temperature, especially with the approximation of the latter to a collapse temperature. Of this pronounced hectic type they form a characteristic accompaniment.

The chills, likewise, present an extreme variability. Now and again they are proportional to the subsequent fever, while in other cases the two phenomena stand apart. At times the rise of temperature is preceded for one or two hours by a slight chilliness, a barely marked gooseskin, a slight shivering. The patient often describes it by saying that he "feels his skin." These phenomena often constitute not only the first symptom of the fever, but of the disease itself. They may also be substituted by a blueness of the nails and a feeling of numbness in the fingers. In cases of fairly high fever the rise of temperature is preceded whenever it occurs, but, as a rule, in the morning hours, by very considerable paroxysms of shuddering and chills.

Markedly intermittent forms of fever, associated with severe chills and sweats, may simulate malarial fever, from which, however, they are distinguished by the fact that they do not return so regularly at the same hour.

Significance.—In general, fever always indicates either a rapid advance of the process or caseation, and is directly proportional to them. Intercurrent and afebrile intervals may be interpreted as indications of a halt. At times, as already stated, it makes its appearance in the initial stage, in apparent perfect health, and reaches a height of 39° C. (102.2° F.) or over, but disappears under rational treatment after days or weeks, to remain away permanently or for a considerable time. If the fever cannot be overcome, it indicates an acute course, and often leads swiftly, within six to ten weeks, to a fatal outcome (*phthisis florida*). Fever in the later stages indicates either an exacerbation of the tubercular process or a breaking-down of tubercular foci. The exacerbation is mostly due to the fact that sputum containing tubercle bacilli in pure culture or mixed with other forms is aspirated into larger or smaller areas of the lung and there sets up inflammatory processes. This condition, like pneumonia, is ordinarily betrayed by a *febris continua*, which may arise acutely, but may disappear again inside of weeks or even days; when the process repeats itself, however, the fever may persist, or, if caseation supervenes, the hectic type may make its appearance.

From thoroughly infiltrated areas, from limited caseous foci or old cavities, relatively few poisons spread into the periphery, inasmuch as the immediate environment, which is to be regarded as the absorption area *par excellence*, has been put by the action of the diffused, concentrated, bacterial toxins into a condition of chronic inflammation or induration. Thus, many cavities can persist for years and not give rise to fever, and, further, the markedly fibrous forms of phthisis mostly run an afebrile course.

With the softening and destruction of the cheesy focus, the picture becomes changed. In case the dead and mortified tissue, the organic debris, and the pent-up toxins find an exit by a large bronchus, the damage to the organism still remains inconsiderable. But in so far as they fail of this exit, are arrested and driven, by the agency of an increased intrathoracic pressure, as coughing, into healthy tissue to become there absorbed, just to that extent does fever occur, higher or lower according to varying conditions. The fever depends on the quantity and specific nature of the matter absorbed, whether tubercle bacilli alone or pathogenic bacteria of a secondary infection. If only a small focus breaks down, the fever may be insidious and hardly noticeable, whereas if a large caseous area be involved, it may become severe, persistent, and pernicious, even to the extent of causing collapse.

How are we to interpret the intermittent fever? Ordinarily it is assumed that the absorption of bacterial toxins goes on continuously, but that they excite the temperature center only when they have attained a sufficient concentration in the blood to produce a cumulative effect. It seems more natural to me to suppose a discontinuous absorption of such a kind that the poisons are taken up into the blood in a certain amount, and then elicit a symptom-complex which we comprise under the name of fever. This consists in a dilatation of the internal vessels, including those distributed through the lungs, and, on the other hand, in a partial and incomplete constriction of the peripheral vascular system. Two effects follow upon this. In the first place, there follows a diminution in the loss of body-heat and a consequent rise of body-temperature; simultaneously, the pressure in the pulmonary veins and arteries is reduced and the absorption of foreign material is at once diminished. Thus, during the fever period the blood absorbs less poisons for the time, while excretion continues to dilute them. The natural result is that in time, perhaps a few hours, the blood becomes to a certain extent purified, the dilatant action upon the vessels of the internal viscera is arrested, the blood-pressure rises, absorption proceeds again in a heightened degree, and, finally, the entire procedure repeats itself *da capo*.

Further, how is it to be explained that the rise of temperature ordinarily occupies the evening or night hours? If we practise an injection of tuberculin, the effect is manifest, not as in morphin after a few minutes, but only after a number of hours, varying with idiosyncrasy, so that a morning injection takes effect in the afternoon or night. Tuberculin, in other words, exercises not an immediate, but a remote influence upon the vasomotors; it thus inhibits autoregulation of the temperature at one level, as occurs, for example, in the thermoregulators of our incubation apparatus. If, then, it be permissible to make a restricted comparison between tuberculin injections and natural absorption, it would seem probable that this absorption is active, for the most part, during the morning and day hours, and in reality this is the case. For activity of itself undoubtedly favors absorption, whereas quiet reduces it. Indeed, we employ rest empirically as a therapeutic agent in the fever of phthisis, and, on the other hand, we observe that activity and excretion increase the fever. At night, therefore, absorption is in general diminished; in the morning, when the patient awakes, he has his paroxysms of cough, and so increases the intrathoracic pressure; he goes through the unavoidable activity and exertion of performing his bodily functions, of washing and eating, and absorption takes place in an increased degree. It is rendered the more abundant by the fact that the secretions have become collected overnight on account of the dulling of the reflexes.

The *febris continua* of acute processes might also be explained, in addition to the enhanced absorptive capacity of a freshly affected area compared with the wall of an old cavity, as due to such an overproduction of the toxins that even with reduced blood-pressure enough is absorbed to maintain the temperature at an abnormal height.

Consequences.—The importance of the fever lies essentially in its injurious influence upon the entire organism in case it persists for any length of time. It is only exceptionally that patients do not exhibit the effects of protracted fever to a marked degree. The fever induces in the already sparely nourished frame of the invalid a heightened consumption of albumin and tissue material, and in this manner brings about considerable losses of weight, which are generally proportional to the height and duration of the temperature. This action is aided by the occasionally serious disturbances of appetite. *The loss of weight again facilitates an increase of absorption, and with it fresh rises of temperature.* Only with a low grade of temperature can the increase of combustion be compensated by abundant nourishment, and thus even an increase of weight be achieved.

As further injurious effects of the fever, we must mention in particular the weakening of the heart, the loss of strength through profuse sweating, and the unhappy influence upon the spirits of the patient. These evil effects are not to be measured entirely by the height of the fever, but depend very largely upon its duration, whether it persists only for several hours or for half a day and the night. In other words, the important element is the number of calories which have been formed and added up. It also varies with the nature of the temperature curve, whether the exacerbations and remissions are gradual or sudden. Peter determined a local rise of temperature upon the affected side, a finding which some authors have confirmed and others have contradicted.

[The relative trustworthiness of oral and rectal temperatures has been studied by a number of observers. Fanning and Champion,* and Franck† recommend the rectal method as decidedly the more reliable. Kelynack and Williams,‡ on the contrary, conclude, after investigation, that oral temperatures, if carefully taken, are reliable for practical purposes. The general observation of the profession, however, as a result of experience, is decidedly in favor of rectal temperatures. Schroeder and Bruhl§ claim that in normal persons, after considerable bodily exercise, there is a slight rise in the rectal temperature; that in cases of tuberculosis this rise also takes place, but often to a less degree than in health. But in healthy persons the temperature falls again to normal in about half an hour, while in tuberculosis the fall requires a longer time.—Ed.]

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* Lancet, April, 1903.

† Therap. Monatshft., May, 1903.

‡ Brit Med. Jour., Oct. 24, 1903.

§ Münch. med. Woch., Aug. 19, 1902.

CIRCULATORY APPARATUS.

The heart and vascular system contribute a very prominent and at the same time frequent symptom in phthisis—namely, *acceleration of the pulse.* In so far as fever is present, an abnormally frequent pulse is explained thereby. Often, however, the pulse-rate rises independently of the fever; this occurs, especially in young individuals, in the first stages, as a prodromic symptom, and as such may awaken a suspicion of phthisis, and so become of diagnostic significance.

At first the pulse is only slightly excitable, and increased in frequency. Only after meals, after insignificant bodily exertions (bending, walking, prolonged standing), or psychic emotions, as also toward evening, does it exhibit a frequency of 90, 120, or more beats. It often exhibits a peculiar wavy tremulous character. Later on, with the advance of the disease, the rapidity of the pulse often persists even during rest, becomes habitual, but is still subject to further acceleration by the previously mentioned factor. The patient is often unaware of this condition. At other times there goes with it palpitation of the heart, which disturbs the patient and robs him of sleep, or an actual delirium cordis, or a certain anxiety, or dyspnea. The rapid pulse is generally weak, soft, compressible, and lacks the tension of the pulse of inflammatory fever.

Etiology.—As is well known, pulmonary tuberculosis is ordinarily associated with enlargement and caseation of the bronchial glands, which often press upon the vagus nerve. In a number of cases the autopsy has, in fact, shown compression of the vagus, single or bilateral, by the swollen or caseous tracheal and bronchial glands. Tachycardia as a symptom of tuberculosis of the tracheobronchial glands has been emphasized by various authors (Becker, Rilliet and Barthez, Gueneau de Mussy, Pröbsting, Pelizaeus, Riegel, Maixner, Guttmann). In some cases the phenomena were so marked that death came with symptoms of dyspnea, cyanosis, and edema. Merklen and Jouanneau report such cases. Besançon records a case in which a phthisical female of thirty-three had a pulse of 160, with a temperature of 37.8° C. (100° F.). Symptoms of asystole supervened, with severe dyspnea, cyanosis, edema, albuminuria, reduction of urine to eventual anuria. Digitalis and caffein had no effect. At the autopsy, in addition to pronounced lesions in the lungs, the tracheobronchial glands were found much enlarged, the left vagus slightly above the region of the recurrens was overgrown by enlarged lymph-glands, and the heart was small, soft, with no valvular lesion.

The observation of many authors that individuals with a rapid pulse are predisposed to tuberculosis should probably be modified so as to read correctly that such individuals already possess tubercular tracheobronchial glands and that the pulmonary symptoms come into evidence only later.

Compression of the nerves may be caused, in addition to the swelling of the tracheobronchial lymph-glands, by mediastinitis, pleurisy, and pericarditis. Thus, in one case Jouanneau observed a tachycardia which resulted from compression of the phrenic and vagus nerves by pleuropericardial adhesions at the base of the heart. Now and again the inflammatory process travels from the left apex to the upper portion of the pericardium, in which a small rapid pulse often results. Tachycardia through compression of the vagus is well known to occur in other diseases, such as carcinoma of the glands, carcinoma of the mediastinum, enlarged glands in pseudoleukemia, and hypertrophic glands after diphtheria (Jacquet).

In compression of the vagus, which is a cardio-inhibitory nerve, we ought really to expect not an acceleration but a slowing of the pulse, if we regard the compression as an irritant. As a fact, slowing rarely occurs. Destruction or section of the nerve produces acceleration. The fact that the presence of the glands has a similar action is to be explained by the very gradual stimulation; thus, for the sake of comparison, a blow on the ulnar nerve elicits a violent reaction, whereas a slow steady pressure puts the arm to sleep.

Marfan ascribes the tachycardia of tuberculosis in part to a general diminution of the caliber of the air-passages, basing this theory upon Marey's law that breathing through a narrow tube causes diminution of respiration and acceleration of the heart.

At times there is a neuritis of the vagus. Vierordt has contributed a case of polyneuritis in which the vagus was implicated with atrophy of a large number of nerve-fibers. The frequency of peripheral neuritis in tuberculosis has been emphasized by Pitres and Vaillard. The affection may involve any of the nerves, especially those of the limbs, of the brain, the phrenic and the vagus.

In addition to this purely mechanical factor, the acceleration of the pulse is also partly attributable to the fall of the blood-pressure, which is almost constant in phthisis. Marfan failed to find it in only three out of one hundred patients, and in these three there was arteriosclerosis. The blood-pressure may be lowered very early in the disease, apparently through the depressant influence of the toxins of the tubercle bacilli, and of the secondary bacteria upon the circulation. A similar action of bacterial poisons, whereby acceleration of the pulse is produced independently of fever, occurs also in other infectious diseases, *e. g.*, diphtheria, influenza, and typhoid (Bernheim). Bouchard isolated a body with pronounced vasodilating action from tuberculin. Similar bodies have been found in pyocyaneus by Romberg, Charrin and Gley, and in staphylococcus by Arloing.

The softness of the pulse is due in part, also, to the vasomotor irritability of phthisis, which betrays itself by the facial flushing upon the slightest occasions of physical or of psychic nature. Finally, it depends upon the weakness of the heart due to the action of the toxins of the tubercle and mixed bacteria.

Heart weakness is one of the most serious consequences of phthisis, and not rarely constitutes the actual cause of death. At first it appears only as a functional trouble; one hears occasionally during excited heart action a systolic murmur, especially at the aortic orifices; later on it often is associated with an anatomical defect, inasmuch as the heart partakes of the general emaciation, and, under the combined influences of malnutrition, anemia, and fever, undergoes atrophy. Bizot found the heart in fatal cases of phthisis smaller than in other bodies. The same fact was observed in two-thirds of the cases by Andral, Louis, Rokitansky, and others. Brehmer interpreted this diminution of the heart's size not as a result, but as a forerunner, as an etiological factor, of phthisis. In other cases there is the picture of fatty degeneration, which is also to be explained as a consequence of the action of the same agents and of the hindrance to circulation.

Dilatation of the right ventricle, with or without insufficiency of the tricuspid, also results both from the obstructed blood-flow, which increases the tension in the pulmonary artery, and from the diminished resistance of the cardiac musculature. Portal has drawn attention to this fact. Jaccoud believes that it occurs especially in the cases with marked cavity formation, unless hemoptysis produces an equalization of pressure. Brun asserts that he has observed it in cases with a rapid course, whereas, in more gradual cases, an anastomosis between pulmonary and bronchial arteries occurs. Bard, Lienard, and v. Sokolowski emphasize its frequency and credit the pronounced forms with insufficiency to the chronic fibroid type of phthisis with coexisting emphysema. A remote consequence of such insufficiency is the congestive condition of the liver, the kidneys, and the extremities. In how far the dilatation and insufficiency, the frequency of which is disputed by many writers, are due purely to the anemia is undetermined; certain it is that the anemia produces such a result of itself.

Through compression of the veins venous swellings are produced on the chest, shoulders, and neck; cyanosis of the face (lips) and of the nails results and asthmatic dyspnea oppresses the patient. Concerning the tuberculous diseases of the circulatory system see "Distribution."

SKIN.

The skin often becomes pale early in the disease as a result of the anemia and the malnutrition; it shows the subcutaneous veins, changes color easily, and becomes fawn-colored or grayish, wrinkled, dry, shiny, and scaly. With every intense circulatory disturbance it acquires a livid and cyanotic appearance, and easily perspires.

In rare cases, with concurrent fatty infiltration of the liver, the sebaceous glands become fatty, and the skin has a greasy, smeary, or, according to Frerichs, velvety character (Gabler).

Frequently, as compared with other individuals, and often very early, the breast, back, and belly become covered with yellowish-brown, dusky, slightly raised spots, which are at first lentil-sized and later become confluent. They give the body a peculiar spotted appearance, and show branny desquamation upon being scratched. This is pityriasis versicolor, a parasitic growth of the microsporon furfur discovered by Eichstedt, the development of which is highly favored by the frequent sweats and deficient cleanliness of the patients. As it produces no discomfort, or only moderate itching during perspiration, it is ordinarily not further noticed. The assumption of a direct connection between pityriasis and consumption is not justified, notwithstanding the positive inoculation experiments of Daguet, Hericourt, and Barduzzi. Their results are attributable entirely to faulty technic.

At times, also, the forehead and cheeks show light-yellow shiny, non-desquamative pigment spots, the so-called chloasma phthisicorum, which signify intestinal complications (Gueneau de Mussy) or changes in the spleen and lymph-glands (Jeannin).

When the disease has reached an advanced stage, there occurs, as in other wasting illnesses, pityriasis tabescentium. This is a desquamative process due to desiccation and atrophy of the skin; the scales are far larger than in pityriasis versicolor, and lack the characteristic color and the sharp contours of the latter.

The toes and especially the digital joints are not rarely found to present nodal thickenings. The nails, brittle, at times cyanotic, become longitudinally curved, and claw-like. This "drum-stick" shape has been shown by *x*-ray investigations (Litten and others) to concern the soft parts alone as a rule, while the bones are not implicated. It is in nowise characteristic of consumption, but occurs in a far more pronounced degree in diseases associated with considerable cyanosis, such as the inherited or acquired heart diseases, in other chronic lung troubles, bronchiectases, empyemata, etc. In pulmonary phthisis it develops only in the very chronic forms. The phenomenon is attributed to obstruction of the venous circulation (?).

In the hair, too, degeneration is evident. It loses its gloss, becomes dry, atrophic, splits, falls out, and loses its pliability and strength, as is shown by tests of its tensile capacity. Now and then premature grayness is observed.

A characteristic condition of the margins of the gums in phthisis has been repeatedly described and credited with diagnostic significance (Fredericq, Thompson, Dutcher). Thompson described its color as red in acute tuberculosis, bluish-red in chronic tuberculosis, white in scrofula, livid in old age, chronic abdominal disease, and malaria. The broader and redder the margin, so much the more acute was the course supposed to be. Sticker investigated the gums in 1000 invalids of all kinds and asserts that he found them reddened almost without exception in phthisis. Especially in young individuals, he believes that this phenomenon is one of the earliest symptoms of tuberculosis. In pregnancy this condition is of irregular occurrence. In non-phthisical invalids it occurs only exceptionally and in old age. Andreesen discovered the symptom among 800 invalids in 92 cases, of whom 69 had pronounced tuberculosis with the bacilli in the sputum, and 23 were more or less suspected of the disease. According to others, this symptom possesses no especial significance, since it is not always evident in phthisis, and, on the other hand, occurs also in other diseases.

At times herpes zoster is found with consumption, and gives premonition long in advance by occasional attacks of pain; as a rule, it also lasts longer than an ordinary herpes. It originates either through inflammatory extension of the disease, and is then situated upon the thorax; or as a result of the action of the toxin, and then arises in other parts of the body (Rendu, Huchard).

Edema of the subcutaneous tissues occurs, if at all, usually toward the end of life, and is caused by cardiac weakness, in certain cases by the intercurrence of cardiac insufficiencies, and by the hydremia of the blood. The result of these conditions is a peripheral venous stasis. Most often the edema involves the ankles first, and at times there may be even a thrombosis of the saphenous or femoral veins. Frequently edema is the first indication of amyloid degeneration of the kidney.

Aside from its cardiac and hydremic origin, such edema often results from neuritis, as, for example, in the cases of Venn, Strümpell, and Pal. The last-named author finds that the edema and the coincident diminution of faradocutaneous sensibility constitute at times the only clinical expression of the so-called neuritis of tuberculosis. All other symptoms may be lacking.

An extremely rare phenomenon is cutaneous emphysema. It is believed that a sudden violent increase of pressure produces a rupture of the ultimate bronchioles and of the alveoli, and that air penetrates through these into the interstitial tissue. This emigrated air then travels either along the pleura or along the bronchial tree to the trachea, and so to the tissues of the neck. As the result of successive paroxysms of cough, more and more air is driven into the interstitial tissue of the lung, and from there into the subcutaneous spaces, until finally the entire thorax, the arms, and even the legs, acquire the customary doughy feel, and give crepitation upon pressure (Fräntzel). An analogous subcutaneous emphysema is seen in pneumothorax, when the costal pleura suffers a lesion of continuity either through the action of tubercular ulcers or by means of the introduction of an aspirating needle, also without external injury in phthisical patients, if a cavity ruptures through the pleura into the subcutaneous tissues, as in the case of Pascheles.

In a case of phthisis observed by Fräntzel, the trouble arose from an emphysema in the anterior mediastinum and trachea, which could be followed out in the left lung to the finest bronchial twigs. Here the distended emphysema blebs, arranged like a string of pearls which lay between intact alveoli, terminated in the very narrow twig of an apparently closed bronchiole. This brought about a pronounced subcutaneous emphysema over the entire thorax, neck, and arms, even down to the hands, and also in the upper part of the thigh. In a second but less pronounced case, the emphysema disappeared after ten days.

SWEATING.

The disturbance in the activity of the skin is revealed by a more or less abundant secretion of sweat, which may even present itself at a fairly early period, before the physical signs are evident. This is a phenomenon which often attains an importance hardly equaled in any other disease. The sweating is, as a rule, proportionate to the severity of the disease, or rather to the acuteness of its course. In the earlier stages it is often not very pronounced, especially if there be no emaciation. It appears, and, as the process becomes quiescent, again disappears. In chronic processes it is often absent until the final stages. Louis failed to find it in one-tenth of the cases.

At first the tendency toward sweating manifests itself only as a clamminess of the skin, which especially affects the forehead, hands, and feet. After slight excitement, exertion, or short walks the extremities become cold and moist. Often the patient hardly notices the fact. Night-sweats may also pass unnoticed, if the head and clothes dry up before morning. Night-sweats occur, as a rule, toward morning, at about five o'clock, sometimes even earlier, from two to three, after the first nap, or shortly after falling asleep. Von Limbeck, on a basis of four observations, puts the maximum of night-sweating at the beginning of the night's sleep. The patient awakes and finds the sacrum, breast, forehead, and throat moist, and finally the entire body is in sweat. Or he may wake up and feel very warm but not sweaty; shortly thereafter the sweat breaks out, even before he is fully awake. Often a deep, unpleasant dream precedes the sweat.

Sometimes the patient has an instinctive dread of the sweat and becomes exceedingly anxious about it. Many patients are able to inhibit or to cut short the sweat, in case it has not become too profuse, by getting up and changing their night-clothes, or by walking up and down the room several times. If the attack starts in very severely, or is already well advanced, or becomes worse by leaps and bounds, these maneuvers of the patient are of no avail. The patient then wakes up bathed in sweat as though "plunged into a tub," body and linen soaking. He changes his clothes, lays fresh bedding, and falls asleep exhausted. In a short time he wakes up again, and the same procedure repeats itself. This may occur several times during the night, so that the patient dreads going to sleep.

The sweats become more profuse as the disease progresses. Eventually they occur even during the daytime, after brief naps or the slightest exertion, and the strength of the patient is sorely taxed by them. At times the sweat is confined to the anterior surface of the body. In rare instances, I have seen a distribution exclusively or predominantly unilateral. Not infrequently there are also secondary eruptions of sudamina.

Etiology.—The cause of sweating has been variously explained. According to Traube, in addition to the anemia and the fever, a great deal of importance is to be attached to the diminution of the respiratory area, inasmuch as the latter, in conjunction with the skin and the kidneys, is responsible for the secretion of the body-fluids. E. Smith believed that the sweats depended upon the condition of the pulse and respiration. His conclusions, which were based on numerous observations, are in so far of value that they led to the use of wine and nourishment to abort the sweat, a measure which is still in favor in the form introduced by Brehmer, namely, milk with cognac. According to Smith, the pulse sinks normally at night; in phthisis there is an abnormally high frequency during the daytime, and an even relatively greater decline at night. Smith and Brehmer regard sweating as a result of bradycardia, and consider it an evidence of exhaustion. Their treatment is a corollary of this interpretation.

Other writers have attributed sweating to an impeded elimination of CO_2, with accumulation of the gas in the blood, and irritation of the sweat centers. It is certainly erroneous to compare the sweating in phthisis with that of convalescence from other exhausting diseases, and to ascribe it to anemia. The sweating in the former often occurs in the earliest stages, long before there is any suspicion of real disturbance in the composition of the blood.

The striking coincidence between phthisical sweats and sleep has been attributed to insufficient oxygenation of the blood, with imperfect oxidation of the circulating compounds which have a specific stimulant action on the sweat-glands.

It seems very probable that there is an intimate relation between sweats and fevers. As a fact, most cases of sweating also present febrile temperatures, which may, however, elude the physician who contents himself with only three measurements daily. Fever under any circumstances is apt to be accompanied by sweating, and the same general rule holds true also of phthisis. The most profuse sweating generally accompanies the remission in the fever, especially if there be a rapid decline. The degree of sweating is, however, not always proportional to the height of the fever; moderate temperatures are often accompanied by very profuse sweats. It would be going too far to regard the fever as a necessary preliminary to the sweating, inasmuch as we are acquainted with other conditions which are capable of producing it without affecting the temperature.

It seems to me most in harmony with the phenomena to look upon the sweats of consumptives as due to the absorption of the proteins of the tubercle bacilli, and, in some cases, of the secondary bacteria. The poisons are taken up into the circulating blood and exercise an irritant action both upon the heat centers, thus producing fever, and also upon the sweat centers in the cord and medulla and the peripheral secretory glands. This explanation also accounts for the fact that, notwithstanding the greater disturbance, the diminished excretion of fluid, and the increased difficulty in the elimination of CO_2, which characterize a chronic course of the disease as compared with an acute phthisis, the secretion of sweat is incomparably less in the former, owing solely to the more gradual absorption of the poisons.

Often both of these reactive phenomena, the sweating and the fever, go hand in hand, while in other cases one or the other of the two predominates. This may depend in part upon individual idiosyncrasies, especially upon a relatively increased irritability of either one of the centers. Perhaps, too, the various species of associated bacteria, the action of which is still rather obscure, have a share in altering these reactions. Even in health there is an enormous variability as regards sweating. Some persons retain a dry skin, notwithstanding inordinate exertion in the heat of the sun; while others sweat profusely upon the slightest effort. The weaker and more anemic the individual, the greater, as a rule, is the tendency toward sweating; hence it is especially marked in advanced phthisis. In youth, in which absorption is more rapid and the febrile reaction in all diseases is more pronounced, the sweats are especially profuse. Now and again sweating and diarrhea seem to complement and replace one another in phthisis. Indeed, the same phenomenon normally characterizes the reaction to fear or anxiety.

It seems very unlikely that the sweats are to be regarded in the nature of a defensive effort on the part of the organism, as an effort to eliminate the toxins. On the contrary, even laymen regard them as ominous, on account of the exhaustion and general disorganization which accompanies them, and the great improvement which follows their suppression.

The sweat does not carry infection. This fact, which was *à priori* probable, has been demonstrated by means of a special research of Mattei's. Sweat taken from the bodies of uncleanly consumptives did, indeed, contain tubercle bacilli, which were capable of reproducing the disease when inoculated into animals, but this was very evidently due to accidental contamination with sputum. If the precaution was first taken to clean the patient thoroughly, both microscopic examination and inoculation of the sweat yielded a negative result.

MUSCULATURE.

Like the skin, the muscular system becomes markedly atrophic during the course of phthisis. In this condition it exhibits increased irritability. A certain phenomenon to which diagnostic value has occasionally been attributed deserves especial mention. I refer to the so-called idio-muscular contractions, which Schiff first observed in the exhausted or moribund muscles of animals. If the pectoralis major of an emaciated consumptive be percussed, instead of the normal lightning-like contraction there is a welt-like swelling of the fibers under the percussing finger, which lasts for a brief period and then disappears. At times a sluggish, undulatory, muscular wave starts from this welt and travels to each of the extremities of the muscle (Auerbach). Lawson Tait ascribes pathognomonic value to this symptom in phthisis; this is denied by von Millbacher, Stadelmann, and von Ziemssen. It is, indeed, more frequent in phthisis than in any other condition, but may occasionally occur in a number of other diseases when associated with much emaciation, *e. g.*, in typhoid in the fourth to the fifth week (James), or with neoplasms, etc.

Idio-muscular contractions take place when the fat cushion has been entirely absorbed and the muscle itself has become highly atrophic. They are especially elicitable in muscles which lie directly upon bones; for example, the pectoralis major, supraspinatus and infraspinatus, deltoid, and triceps. Histologically, the primary bundles are atrophic, and show fatty degeneration. There are also proliferative processes in the perimysium internum and in the interstitial connective tissue, multiplication of the nuclei in the sheaths of the smaller vessels, and thickening of the adventitia of the larger vessel.

ALIMENTARY TRACT.

Stomach.—Gastric disturbances are frequent in phthisis, though not invariable. Often they are the earliest symptoms, but subsequently disappear, only to recur again in an altered form. Marfan and others are therefore justified to a certain extent in describing the gastric phenomena as those of the early and the late stages respectively. Many consumptives retain a healthy appetite for years, in spite of fever and advanced disease. This may last until the very end. It is really marvelous to see the enormous quantities of food which are not only eaten, but really digested, by some patients. Sometimes there is a real desire for the food, while at others there is a notion that overfeeding will hasten recovery. One of my patients in Görbersdorf complained bitterly that he had indigestion and could eat only four beefsteaks at supper. These patients are mostly those who have been powerful individuals and healthy eaters from their youth; they are able to put on considerable weight in spite of occasional febrile attacks. As a rule, they have a slowly progressive form of the disease, perhaps just on account of their overeating. Some, however, fail to profit from their food and the consumption moves inexorably forward.

In the majority of cases—two-thirds according to Bourdon, one-third according to Hutchinson—there are manifestations of disorder of the alimentary tract—anorexia, indigestion, nausea, distention or vomiting. Marked anorexia, a real *crux medicorum,* is often an early symptom.

In some cases there is aversion only for the ordinary articles of diet, or for certain particular dishes, generally those most digestible, while delicacies are not refused. In other cases, again, there is absolute dislike for all articles of food, which may even amount to disgust. Or, again, the patient may sit down to table with a good appetite, even with hunger, but after a couple of mouthfuls feels sated and can swallow nothing more—his esophagus is as though "tied together." I have repeatedly found that all these gastric symptoms by preference attack such patients as have always been small eaters, or those who have previously experienced successive attacks of gastric disorder, while those are generally spared who have previously given much time and attention to the pleasures of the table.

If the anorexia is an early and prominent symptom, and precedes the characteristic signs of the disease, namely, cough and expectoration, the patient is often apt to regard his whole trouble as a gastric disorder. The physician, likewise, may not escape this error.

The occurrence of these symptoms at a time when anemia and fever have not yet wasted the body would seem to indicate some other etiological factor. The most probable assumption is that certain chemical compounds, the proteins, are taken up into the blood, and secondarily produce these irritative phenomena. In rare cases there may be direct compression of the vagus by swollen glands (Gueneau de Mussy, Peter), which should then manifest itself by the other signs of such compression, namely, irritative cough and tachycardia. Fever, too, generally, though not invariably, affects the appetite.

It is remarkable that the functions and secretions of the stomach may continue normal during the development of these symptoms. The condition is therefore an anorexia nervosa. Isolated observations of this condition were first made by Cahn and von Mering, Ewald, Edinger, Glucinski-Wolfram, and others; and these were followed by the more extensive investigations of Brieger, Klemperer, Schetty, Immermann, Hildebrand, and others.

In general, the disturbance of the stomach runs parallel with the course of the disease. Thus, Brieger found that at the beginning of the disease only half of the cases had a normal gastric juice—in cases of medium severity 33 per cent., and in severe cases 16 per cent.; the rest had a more or less pronounced insufficiency. Klemperer's investigations revealed a practically normal condition of the secretory and motor functions in the latent stage of the disease, frequently hyperchlorhydria in the initial stage and in the terminal stage hypochlorhydria or anachlorhydria, with pronounced motor insufficiency and dilatation, and fermentation of the food. On the other hand, in the consumptives investigated by Immermann and Schetty, embracing all types, both those with and those without gastric symptoms, gastric insufficiency and hypochlorhydria were absent; indeed, the opposite conditions sometimes prevailed. Brieger could not demonstrate any relation between the fever and the secretion of HCl. Hildebrand regularly detected free acid in afebrile cases, but found it absent in those which ran continuous fever. By reducing the temperature by antipyretics, he could restore the acid in the gastric secretion.

The anorexia is often accompanied by a sense of fulness after meals, even when little has been eaten, by a certain tenderness to pressure in the epigastric region, by discomfort or even pain in the stomach and intestines (dyspepsia nervosa).

One of the most unpleasant phenomena is the frequent retching and vomiting of consumptives. With this, too, the functions of the stomach are at first perfectly normal, the gastric juice satisfactory in quantity and quality, and there is no motor insufficiency. Now and again, however, there is a pertussis-like attack; the patient begins to retch and the stomach surrenders whatever it happens to contain—gastric juice, mucus (often reflexly increased in amount), or undigested food.

This retching and vomiting seems to result not so much from any real gastric disorder, but rather from the violent abdominal compression due to coughing. It is not dyspeptic, but motor, and naturally occurs more easily with a full than an empty stomach. It may be compared with the involuntary passing of urine after coughing which many women exhibit. It frequently accompanies the morning "pulmonary toilet" of consumptives. It depends entirely upon the time of breakfast, whether this is vomited or not. Sensible individuals wait until they have finished with their *vomitus matutinus* before they take their breakfast. Often the cough and retching seem to depend on nasopharyngeal catarrh, and are both eliminated with the cure of this condition.

The cough appears in many cases to originate from the stomach—the so-called stomach-cough. The physiological basis of this condition is somewhat obscure, but its existence is not to be flatly denied. Many patients, including some well trained in self-observation, complain that they cannot eat a fairly good meal without being immediately compelled to cough. This cough may pass away or may lead to an attack of vomiting. This condition is entirely independent of gastric insufficiency, as is shown by the absence of nausea and of coating of the tongue. Many of the cases are able to enjoy a fresh meal very shortly after the vomiting has passed, and so replace what they have lost. In all probability this form of vomiting is due to gastric hyperesthesia. Anorexia and vomiting are intercurrent affections; they show remission,—they come, go, and return.

In contrast to the above set of symptoms, which are largely nervous or mechanical in origin and accompany the initial stage of the disease, is another series of phenomena which characterize the later stages. They constitute a very severe affliction for the patient, and often hasten his exitus.

Here, too, vomiting is pre-eminent, but very different in character. Very soon after eating, sometimes even before, there is nausea, with eructations of bitter, acid, pungent, often badly tasting material, which produces vomiting, with or without cough. There is an absolute aversion to taking another meal. There are also other symptoms of disturbance in the gastric functions. The walls of the stomach suffer with the rest of the muscular system from the effects of the general debility and anemia. The organ becomes atonic and distended, and the motor functions are delayed. The mucous membrane also becomes inflamed both as an expression of the general disorganization, and also at times as a result of a too energetic course of feeding. Frequently the gastric catarrh is traceable to the habit of swallowing sputum in large quantities, which does not indeed directly infect the organ, but tends to produce hypopepsia and fermentation by means of the toxins which it carries (Marfan). In rare cases the gastric symptoms are determined by amyloid degeneration of the walls (Edinger).

Fungus stomatitis occurs in the final stages of phthisis, just as in other forms of cachexia, *e. g.*, cancer and diabetes, and is generally the precursor of death. The well-known symptoms—namely, thick coating of the buccal mucosa, sharp burning, a sensation of dryness, and difficulty in swallowing—render the sad picture of suffering still more sombre.

Intestinal Symptoms.—The intestinal functions and defecation are, as a rule, normal, especially in the chronic form of the disease, and may remain so until death, or at least until the last few days. In not a few cases the marked hyperchlorhydria of the earlier and milder phases of the disease is the cause of great sluggishness in the lower bowel. When the pulmonary foci have become more extensive, especially in the so-called third stage of the disease, and in very acute cases, diarrheal movements frequently occur. This symptom is very variable; the diarrhea may disappear after a short time, or may alternate with periods of constipation, or may continue until the time of death. It may be associated with severe pains, often located in the region of the cecum and the hypogastrium, or with attacks of colic, and may be the source of much suffering. The causes of the diarrhea are various. Aside from the intestinal affections, which are accidental, and which occur in phthisis just as they would in a healthy state, the essentially phthisical diarrhea is due chiefly to the voluntary or involuntary swallowing of sputum.

In the chapter on infection we explained that the gut does not ordinarily become infected as a result of the ingestion of the bacilli, especially when they are enveloped in masses of mucus, as in sputum. Continued exposure of this kind may, of course, eventually overcome its power of resistance. The sputum may, however, exercise a purely irritant action, resulting in irritation of the mucosa and mucous catarrh, just as it does in the trachea and bronchi. These changes are due, not to a local tuberculosis, but to the action of the proteins and of the accessory micro-organisms. The proteins are evidently not destroyed in the stomach, since that organ itself suffers from their effects.

The intestinal mucous membrane does not suffer either as early or as severely as does that of the trachea, because the sputum is enveloped and diluted with food and drink. It is proper in this case to speak of a dilution, inasmuch as soluble bodies are in question, not corpuscular elements or bacteria. At times, especially at night, when the patient is too comfortable to expectorate, there is a steady overflow of sputum into the gut. It is easy, therefore, to understand that consumption may produce an intestinal catarrh, especially if the pulmonary process be of long duration and characterized by profuse secretion. The intestinal process is, however, not necessarily tuberculous in nature; it may be a simple irritative catarrhal inflammation. In this connection the pathological findings of Girode are of interest. He described various changes in the structure of the gut, which involved notably the glands and the lymphatic structures. The fundus of some of the glands of Lieberkühn was seen to send hollow prolongations into the depths of the mucosa, as far down as the muscular coat; a secondary glandular layer was thus formed which bore considerable resemblance to an adenoma. Further, in 29 autopsies Girode found tuberculous lymphangitis nine times. The subserous lymphatics stand out with especial clearness; the intermuscular lymphatics are degenerated and narrowed. At times there is complete obliteration through stasis. The lymphatic trunks in a healthy and intact wall are blocked by white masses, which resemble anemic infarcts. Under such circumstances the absorption and circulation of the lymph naturally meets with difficulties. Not rarely the blood-vessels are obliterated, which gives rise to serous transudation and diarrhea. In four cases Girode found an edema of the gut.

I cannot neglect this opportunity to call attention to the coincidence offered by the obliteration, both of the vessels in the gut and of those in the lung. It seems likely that the tuberculous proteins contain a substance capable of coagulating blood and lymph. This is a factor of some importance in preventing the dissemination of the tubercle bacilli throughout the body.

Girode also calls attention to the rather dark discoloration of the feces, which is to be ascribed to hemorrhage. In the ileum and cecum he found certain discolored areas, light in the center and darker toward the periphery, ranging in size up to a five-franc piece, whose origin he attributed to small and recurrent hemorrhages.

The proteins alone may, therefore, give rise to a variety of phenomena. In the first place, there may be simply an irritation of the mucous membrane, *i. e.*, of the nerve-endings of the sympathetics, with increased peristalsis. Or there may be a catarrhal enteritis. Finally, they may even cause superficial erosions, catarrhal ulcers, of which the peptic duodenal ulcer is an example (Sée). Depending upon their site and their extent, these ulcers have a tendency to cause diarrheas of varying severity. According to Nothnagel, the colon is that part of the gut in which ulceration is especially apt to cause diarrheas. Tormina and colic are to be similarly explained.

In addition to these forms of intestinal disease, which result from the action of the toxins, there is also, and not rarely, a true bacterial infection of the mucous membrane, an intestinal tuberculosis, which may, likewise, cause diarrhea and pain.

A closer description of this and its distinction from changes which are not specific, viz., amyloid degeneration, must be reserved for the chapter on the extension of tuberculous foci outside of the lung.

The proteins reach the gut not only through the sputum, but also at times in the blood. This occurs when the toxic products are absorbed from the lung in very large amounts. Having reached the gut by the vascular route, they may produce a variety of effects. Irritation of the nerve-endings gives rise to a heightened peristalsis, while the glands may be stimulated to secretion. Analogous processes occur in malaria and in other forms of poisoning (Nothnagel). The occurrence of such diarrheas, without the swallowing of sputum, was a notable accompaniment of the injections of very large doses of tuberculin, as they were given, for example, in the year 1890. In such cases we also expect the other symptoms of a protein intoxication, namely, high fever, etc.

The multiplicity of causes often renders diarrhea a very early symptom. At times, indeed, the diarrhea may make its appearance before the pulmonary process has gone on to anything like extensive destruction, or even before there are any real clinical symptoms of the pulmonary trouble (premonitory diarrheas). These are the masked cases of pulmonary tuberculosis, which for a long time figured as forms of intestinal disease. Children, especially, are apt to exhibit this type, because they generally swallow all the sputum. The insane and idiots also swallow their sputum, since their reflexes are too sluggish to prompt them to cough. In this class of patients the entire course of a pulmonary tuberculosis is characterized only by an obstinate and profuse diarrhea, and the extensive lesions of the lung appear as a revelation at the autopsy. There are similar reports from the prisons.

The occurrence of diarrhea, unless it shows itself to be very tractable, is a very serious symptom and one justly dreaded by the practitioner. For even in case it does not signalize the appearance of a fresh focus in the gut, it yet tends to hurry the debilitated organism beyond the reach of help. At times, indeed, one does observe that cough and dyspnea are temporarily improved, and that expectoration diminishes simultaneously with the appearance of the diarrhea. But it would be most delusive to base any hope upon this change. The disease itself advances the more ruthlessly and swiftly in proportion to the loss of nutrition which is entailed by the diarrheal evacuations.

EMACIATION.

The profound disturbance in the animal economy evidences itself by a pronounced loss of fat and an atrophy of the muscles, which put a characteristic impress on the appearance of the patient, and have given the name consumption to the disease. In a large number of patients the loss of flesh is one of the earliest symptoms, and attracts the attention of the physician even before cough and fever have made their appearance. The patient discovers that clothes, belt, or corset are too large. Many a girl rejoices that she at last has attained a slender figure, never suspecting the unfortunate cause.

Loss of weight is, indeed, a constant phenomenon, but varies greatly among different individuals, and even in the same individual at different times. Often emaciation proceeds very gradually and slowly and almost imperceptibly. Many consumptives maintain a body-weight averaging between 170 and 190 pounds, and a well-filled body contour for years, notwithstanding the fact that the disease has not been overcome by them. Such a condition is in marked contrast to the ordinary picture, and is met with especially in the better classes. At times emaciation proceeds with fearful rapidity. In some cases the body-wasting follows a slow, steady, and inexorable course; week after week the scales show a regular decrease of from two to three pounds, so that one must either deceive the patient or keep him from weighing himself, in order that he may not lose all courage. Again, there may be periods, even when the disease has become far advanced, during which the body-weight remains steadily at a certain height, or even increases by 10, 20, or 30 pounds, or actually oversteps the previous normal. Years ago I had a patient who gained 58 pounds in about six months, in spite of a low fever; added five more pounds after treatment was suspended, and eventually recovered. Such events as this ordinarily signify a quiescence of the disease, which may even be permanent; often enough, however, there is a subsequent relapse which denotes a recrudescence of the disease or the caseation of some old focus. Thus, improvement and relapse may alternate during years.

The loss of substances is not confined to the fatty tissues. The blood becomes impoverished. The muscles also suffer—a fact which evidences itself strikingly in the case of the respiratory muscles, which permit the thorax to fall in and become flat, giving rise to the "habitus phthisicus."

Frequently the loss of substance affects one part of the body rather than another—the face, the abdomen, or the extremities. The loss of fat is in proportion to the degree of development of the panniculus adiposus, and the patient may fall to one-third or two-fifths of his previous weight, in case the disease is not interrupted by some fatal complication. The body is reduced to a skeleton and becomes nothing but skin and bones. In some cases the extreme emaciation is marked by edema. Death finally occurs through exhaustion, just as in animals who are the victims of progressive wasting.

The loss of weight is generally amply accounted for by the anorexia and the deficient nourishment. In many cases, however, the patients have good appetites and eat well, yet continually lose flesh and strength. This may be due to gastric disturbances, to frequent vomiting, to profuse diarrhea and sweats, to pulmonary hemorrhage, or, perhaps, to an interference by the proteins with the constructive metabolism of the body.

That the tubercle proteins exercise a markedly inhibiting effect upon the nutrition of tissues is evidenced by experiment. Animals into which emulsions of proteins and toxins have been injected in large amount, rapidly die, with the clinical picture of inanition. An etiological relationship of this sort is also indicated by the parallelism between emaciation and the rises of temperature due to protein absorption. The higher and more continuous the fever, the more rapid is the wasting; in the afebrile periods, as a rule, the patient ceases to lose weight. Indeed, the fever is of itself capable of inducing destruction of tissue by means of the increased combustion and the increased loss of albumin which it entails. The fever is not however, the only cause. In the other infectious diseases fever of the same severity and of the same duration is not accompanied by a similar grade of nutritional disturbance. The emaciation of typhoid is, therefore, not to be considered as a mere consequence of the fever, but both phenomena are in part coördinated manifestations of a single cause,—namely, the absorption of proteins,—and of this process they afford a reliable and valuable index.

URINARY SYSTEM.

In the commencement of the disease the urine is typically normal. The loss of flesh is accompanied by phosphaturia, especially cf the calcium salts, as shown by Benecke, de Renzi, and Senator. According to Teissier, the phosphaturia vanishes with the advent of the period of cachexia. Stockvis attributes no diagnostic importance to this symptom.

The chlorids are excreted in considerable quantities, according to Buchot and Rochefort. The urea is in general diminished, but may be increased by heavy feeding, more especially by overfeeding (Peiper).

Interstitial and parenchymatous diseases of the kidney, due to amyloid and tuberculous changes, evidences itself by albuminuria. In the later stages there may be pus. Tubercle bacilli are not generally found in the urine, unless the disease actually involves the genito-urinary tract itself, as has been shown by Rosenstein, Babes, and Smith.

Hochsinger attributes almost pathognomonic importance to indicanuria in the tuberculosis of young children, but this has been disputed by Steffen, Giarré, and Gehlig.

Ehrlich considers his diazo-reaction to have great prognostic importance; if it were present over a fairly long period of time, he prophesied an early death.

A mixture of 50 cc. of sulphanilic acid solution (ac. sulphan. 0.5, ac. hydrochlor. 5.0, aq. dest. 100.0) and of 1 cc. of a sodium nitrite solution (natr. nitros. 0.5, aq. dest. 100.0) is added to an equal quantity of urine; to this mixture an eighth of its volume of ammonia is added, and the whole thoroughly shaken. The reaction consists in a deep carmine or scarlet discoloration both of the fluid and of the foam. Further investigations of Lövinson, Brecht, Petri, Escherich, Penzoldt, Georgiewsky, Brehmer, Beck, and others have modified the conclusions of Ehrlich to a certain extent. The reaction is, indeed, present in a large number of fatal cases of phthisis, especially during a considerable period previous to death. It is not invariably, however, of evil import. It may also be lacking in spite of very severe exacerbations of the disease.

NERVOUS SYSTEM.

Peripheral Nerves.—The peripheral nerves of consumptives may give rise to morbid phenomena, even though the central nervous system is intact. Neuralgia, hyperesthesia, and anesthesia have been already described in the chapter on "Pain."

The symptoms are very frequently pressure phenomena due to the associated enlargement of the bronchial glands. Pressure upon the vagus gives rise to tachycardia, dyspnea, and cough. Fleischmann observed a remarkable case of laryngospasm in which the recurrent nerve at autopsy was found to be completely embedded in a package of glands. Hoarseness may similarly be caused by pressure of glands upon the recurrens.

In addition to this mechanical factor, the peripheral nerves are subject to the same parenchymatous inflammations in tuberculosis as in other infectious diseases. These various inflammatory processes, generally grouped together as "degenerative neuritis," are due to the action of the toxins absorbed by the blood. Multiple neuritis, which has been carefully studied by von Leyden, is very often found in association with pulmonary tuberculosis (Joffroi, Eisenlohr, Strümpell, Oppenheim, Vierordt, Venn, Pal, and others). Heine, in particular, has frequently found the phrenic affected. Pitres and Vaillard lay great stress upon the frequency of parenchymatous inflammation in phthisis. They distinguish three groups: (1) Cases which pursue a latent course, or betray themselves only by indefinite, diffuse, fleeting pains. The post-mortem examination reveals pathological alterations in the nerves, fragmentation of the medullary sheath, varicosity or atrophy of the nerve-sheaths, more or less complete atrophy of the axis-cylinders. (2) Amyotrophic neuritis, in which isolated or diffuse muscular atrophy forms the marked feature. The atrophy may appear within six days after the onset of the inflammation. The paralysis is ordinarily widely disseminated, involving the muscles of all the extremities, of the back, the neck, the abdomen, and the diaphragm. The entire group of muscles of an extremity is generally not involved, isolated groups being spared, and a certain amount of motion is thus preserved. (3) Finally, there is that form of neuritis which produces more or less disturbance of sensibility, hyperesthesia, paresthesia, anesthesia, neuralgia, etc. In this group are to be classed the thoracic pains, the arthralgias, especially the melalgia of Beau (see page 377), which affects the legs. Here, too, belong muscular hyperesthesia and myalgia, which may either be spontaneous (Perroud) or may be elicited by pressure or by contraction. This may be so severe as to hinder locomotion. Further, there is the hyperesthesia of the skin—dermalgia—which perferably affects the posterior surfaces of the legs, thigh, the upper extremities, and the trunk. Neuralgias may affect the intercostals, the ulnar, median, radial, cervicobrachial, iliolumbar, femoral, or sciatic trunks (Leudet, Perroud, Dreifus, Friot, Landouzy, Peter). Finally, there may be analgesia or anesthesia of certain definite dermal areas which very frequently accompany the advanced stages, according to Rendu; it especially affects the posterior surfaces of the forearms, and is at times associated with paresthesia taking the form of itching, or of a sensation of cold in the nails.

Worthy of mention are the vasomotor disturbances, recognizable in the swift flushes of color, in blushing, in sweating, which often constitute early symptoms of the disease. Edema may also be a symptom of the neuritis of phthisis, and is interpreted by Strümpell as a localized vasomotor disturbance.

Central Nervous System.—Aside from the symptoms of actual focal disease which may mark the general dissemination of the tuberculous process, there is a certain set of general symptoms which depend upon the anemic condition of the brain, and these are present at some time or other in most cases of phthisis (Lebert). We may instance the attacks of vertigo, the cephalalgia, buzzing in the ears, etc. In some cases, however, there is hyperemia, or simple meningitis, or pachymeningitis, or inflammation of the dura with hydrocephalus, which occurs especially in children.

MENTAL SYMPTOMS.

The changes which the mind undergoes in pulmonary tuberculosis are worthy of greater attention than they ordinarily receive. Heinzelmann, who has done much in the way of investigating, and especially of treating, this aspect of tuberculosis, divides the psychic alterations into two groups, not including those which simply presage the approaching dissolution: (1) Emotional weakness. Emotional instability tending toward ecstasy, general irritability, low grade of excitability leading at times to sleeplessness. (2) Mental degeneration. Optimistic attitude of the patient upon the subject of his health, often encouraged, it is true, by the physician. Diminution of the critical faculty. Deficient or abnormal energy for work. Impulsiveness. In some cases vacillation, in others obstinacy. (Anorexia is due rather to the will than to the stomach.)

At the beginning of the disease there is often a tendency to depression, to melancholia, hypochondria, or absolute hopelessness; as the disease progresses, this frequently changes to optimism, the *spes phthisicorum,* which is in marked contrast to the condition of the invalid, and sometimes leads him to excesses. There is something characteristic in this absolute misunderstanding of his own disease, and a colleague has very pithily remarked that he has never known a consumptive who did not order new clothes shortly before his death.

Even physicians cherish these self-delusions. I once treated a colleague who, in spite of fever, emaciation, and hemoptysis, continued to speak in hopeful terms of his "bronchitis," even to within a fortnight of his death.

Characteristic are the inordinately rapid changes of mood. At one moment the patient is in the depths of despondency, and doubts whether he will still be alive a half year or a month later; the next moment he speaks of the proposed alterations in his factory, or his brewery, and of plans for the distant future. "Exalted to the heavens, depressed unto death"—such is the character of the majority of consumptives. Many a consumptive watches his every symptom with anxiety. If he has once had an hemoptysis, he scrutinizes every expectoration for months afterward, and goes into a fit of worry and excitement over every red streak in his sputum. Every word of his physician and his neighbors he interprets unfavorably and broods over it for days. And yet, if one scans him closely, he desires nothing better than to be contradicted and to be inspired with fresh hope. The more one is busied with making light of his sadness, the more thankful he is.

Lack of self-control is noticeable in the consumptive. A contradiction, a harsh word may put him into a passion of excitement, into wrath and fury, or into a flood of tears, though he be thoroughly conscious that his sickness is entirely at fault. On this account his family often have difficulty with him. He lacks will-power. He pledges himself to the most perfect conduct, to maintain the necessary laws of health; he takes his holy oath upon them, and at the very next opportunity to transgress he yields to the temptation. Incredible levity is often the substitute for good nature.

His intellect, in so far as it does not concern his own bodily condition, is for the most part normal. At most there is a diminished endurance, a tendency to weakness in thinking, often a striking weakness of mind. Now and again, however, there is real lunacy, which may last for months, or acute mania. In one woman I observed ideas of suicide which disappeared after four weeks.

At times the psychic functions are so depressed that, as Heinzelmann says, one might infer a general paresis, were it not for the absence of paralysis and the favorable course. Toward the end, in the last days of the disease, there are somnolence and disturbances of consciousness, which Rühle attributes to edema. There may be convulsions, hemiplegias, monoplegias, paresis, aphasias, pronounced delirium, and maniacal attacks. These phenomena are generally the expression of tubercle formation within the brain. In many cases consciousness remains unimpaired and unclouded to the end, whether from the fact that the patient calmly faces the issue, or that he actually cherishes hope in the very face of death.

The causes of this pronounced alteration in the mind are various—the fever, the anemia, inanition, vasomotor disturbances in the brain, and now and then, perhaps, an immoderate use of the narcotics and alcohol. The peculiar environment in which they live undoubtedly plays its part in disturbing the equilibrium of many patients. There is the prolonged sojourn in institutions and health resorts, often for months or years, without any regular occupation, the lack of any intellectual exercise (Heinzelmann), the oppressive sense of a chronic disease. The excess of sympathy with which such invalids are often burdened is also apt to mislead their minds, as Heinzelmann has well pointed out. The chief cause, however, is again the absorption of proteins, which awakens the latent troubles in the brain and shakes its insecure foundations. At the time when we injected tuberculin in large doses, we had occasion to see very marked though only ephemeral aberrations of intellect, which might or might not be accompanied by marked rises of temperature. Under such conditions we can readily understand that preëxistent nervous diseases may become considerably worse under the influence of a pulmonary phthisis, and that a previously latent hysteria, for example, may give rise to such pronounced disturbances as to give a very especial aspect to the phthisis (the so-called hysterical phthisis). The accessory psychoses may for a time completely mask the subjective symptoms of the disease—cough, expectoration, dyspnea, and pain (Griesinger, Kalischer).

SLEEP.

Sleep is frequently normal, and, again, even without the disturbing influences of fever and sweats, often very insufficient. For hours the patient tosses uneasily from side to side, vainly seeking to rest. Often he has attacks of palpitation, dreamy pictures of his misfortune rise before his eyes, and his life seems blackest in the darkness of the night. Toward morning he dozes off into a sort of a paralytic, comatose half-slumber, often associated with slight chills and sweats, from which he is with difficulty aroused. Many consumptives complain of harassing dreams. The sleeper is aware of an impending danger and cannot escape. He finds himself on a stormy sea, in a frail craft, and cannot reach the shore; he stands upon a dizzy precipice, and falls into the bottomless abyss.

STRENGTH; PHYSICAL ENDURANCE.

In connection with the nervous system, mention should be made of the diminution in the strength and in the physical capacity of the consumptive. It is easy to understand that this should occur after the process has gone a certain distance, when the body has become disorganized by fever, inanition, anemia, emaciation, and loss of muscle. Since, however, loss of strength is not rarely encountered at the very beginning of the disease, before these destructive influences can possibly have produced their effect, here too the absorption of the tubercle proteins is certainly the determining agency.

Consumptives frequently show symptoms of this nature weeks before the cough and the other subjective symptoms begin to attract attention. Careful questioning of the patient elicits the fact that there has been an aversion to work, a sort of weariness, a failure to enjoy his business. He has had to sit down frequently, walks and tasks which formerly amused him have become difficult. In the morning, when he awakes, he finds himself more fatigued than the evening before; his sleep does not satisfy or refresh him. His head is not clear; his nails are at times blue. He often has peculiar paresthesiæ of the skin, as though some one were gently stroking it, feelings of creepiness, of pricking, of goose-flesh, of slight chilliness, transient shudders, and yet the body-temperature may not be raised. These phenomena, as initial symptoms, deserve very especial attention.

Some consumptives, especially in chronic cases, stick at their work for an astonishingly long time. This is true rather of those who are forced to save money. Often periods of usefulness alternate with periods of invalidism for years. Many attend to their business up to the very last days, often at the cost of great effort, and even undergo intense strains. As a rule, however, the capacity for work diminishes as the process advances, and eventually renders the patient incapable of following his vocation. It is exactly this factor—the prolonged period of inactivity to which the consumptive is doomed—which determines the great economical significance of phthisis. Exhaustion finally becomes so pronounced that the patient can barely stand on his feet, and that every movement even in bed wearies him. He is "dead tired."

Strength is often maintained for a considerable time even in acute cases. Of the 221 autopsied cases collected by Grawitz from the records of the Prussian army, most of which were acute, 45 did full military service up to fourteen days before death, 19 of them up to one week, and 9 up to six days before death.

VITA SEXUALIS.

It is an old saying that consumptives are sexually very excitable. As a fact, one often notices an increase of sexual desire of the facultas cœundi, which in rare cases may persist even to death, in spite of the progressive destruction and dissolution of the body. Among women this abnormal excitability is more frequent than in men, the passive rôle furnishing an explanation of the free rein given the "facultas."

At times the lack of other business tends to add fuel to the sexual instinct. Heinzelmann cites the example of a young man with advanced tuberculosis who lay in the open air almost all day long, and at night frequently had sexual intercourse with a chambermaid, who became pregnant. At other times the passion is simply part and parcel of the general over-excitability and nervous tension.

I know of a case in which a woman complained that her husband had coitus with her every night, and that for disgust she could stand it no longer, because he became soaked in sweat during the act. In another case a very sick consumptive had coitus with his wife on the very day of his death. Simmonds reports similar cases. The fact too, that children are born some time after the death of a consumptive father shows that functional spermatozoa can be produced in spite of an advanced process. Errors of observation must, of course, be excluded.

At times such excesses are explained by the consciousness of an incurable malady, and by the desire to enjoy what still remains of the pleasures of life, to drain the cup to the dregs (Heinzelmann), or the patient may attempt to deceive himself and others as to his true condition by an artificial energy in this direction.

But it is not in accordance with facts to represent this increase of the sexual powers as the general rule. It may be that such instances particularly impress us, and so become magnified in number. Louis states that the idea of an increased sexual activity is really ridiculous, and Grisolle confirms him. With the vast majority of consumptives pollutions become more infrequent very soon after the onset of the disease, and the morning erections no longer occur. There is often a feeling of emptiness in the genitals, and finally, as the disease progresses, both the desire and the energy for coitus become less, and in many cases diminish to the point of impotence.

The influence of phthisis upon the sexual life of women becomes more manifest from another point of view. The menses become less frequent as a result of the anemia, and often at the very onset of the disease take on a more watery character, become irregular, or cease completely. Only exceptionally do they continue to the end or become more profuse. At times there may be vicarious hemoptyses. In young girls, if the advent of the first menses has been delayed by the disease, the periods show the same variations as does the disease, so that their recurrence is to be taken as a favorable symptom.

The pregnancies are generally normal. Sterility and abortion may occur, just as in other forms of cachexia, when the disease becomes far advanced. And yet a far-gone consumptive may give birth to a normal child, and die a few days or weeks thereafter.

PHYSICAL SIGNS.

INSPECTION.

The early stage of the disease are not associated with any alterations in the external appearance. This fact is to be emphasized on account of the general tendency to look for the signs of disorganization in suspected cases. The patient may be well nourished and apparently in the bloom of health, his entire personality may bespeak strength and vigor, and yet the tubercle bacillus has gone a long way in its ghastly work. As time goes on, the appearance, of course, shows traces of the disease. The features are dulled, the cheeks show a circumscribed flush, the skin becomes pale, at times livid and cyanotic, the venous network appears through it, and the color changes with every emotion and every exertion. The epidermis becomes dull, gray, wrinkled, dry, rough, and scaly. Perspiration breaks out at the least effort, *e. g.*, with the exertion of undressing, or with the excitement of the medical examination.

The external mucous membranes often keep their color for a long time. Later the lips become pale, and the gums often intensely reddened (see page 395).

The yellowish-brown, dull, scaly spots of pityriasis versicolor are often to be seen on the breast, back, and belly; on the forehead and cheeks are the pale-yellow, shiny, unscaling pigment spots of chloasma phthisicorum in the stage of cachexia; pityriasis tabescentium is also met with (see page 394).

The muscles lose their firmness. With the progressive disappearance of the fat and of the muscles the ears stand out from the head, the nose becomes sharp, the cheeks are sunken, the eyes fall back in their sockets and appear weary or peculiarly moist, the sclera is translucent.

The neck becomes thin and seems longer, the sternocleidomastoids form a prominent band on each side of the neck, the pomum Adami is sharply defined, the supraclavicular and infraclavicular spaces sink in, the cheek bones, ribs, pelvic crests, and the joints become more and more prominent. The scapulæ stick out like wings.

The head is bent forward. The invalid seems years older. The hands become pinched, the phalanges of the fingers and toes quite frequently show the drum-stick deformity (see page 395). The hair of the beard and head becomes dry and thin. Towards the end edema also appears (see page 395), and in rare cases there is cutaneous emphysema (see page 396).

It is traditional to ascribe an especial significance to the phthisical habit, particularly the paralytic thorax. This is characterized by a diminished sterno-vertebral diameter, while the length of the thorax from above downward is not infrequently increased. The muscles of inspiration are weak, the intercostal spaces deepened, the angulus Ludovici prominent; the shoulder-blades stand out, the vertebral column is often slightly convex. Many physicians have been inclined to regard the paralytic thorax as the congenital basis of the disease, and have believed that individuals so formed are actually predestined to contract it. Careful observation reveals, however, that the paralytic thorax is very often not especially prone to contract the disease. Furthermore, a vast number of consumptives do not present this anatomical peculiarity. Finally, it appears that in many cases this characteristic deformity of the chest does not precede the disease, but is rather the result of it, being due to the loss of the supporting tissues, especially the muscles and the fat. Such is the case preeminently in young individuals, in whom the walls of the thoracic cage are more flexible and malleable. The paralytic thorax is, therefore, not a forerunner, nor even a contributing cause of the disease, but only a secondary manifestation which, even at that, is not very frequently encountered. It is not, however, invariably associated with phthisis, but may occur independently of the disease.

Even at a time when pulmonary phthisis was regarded as a constitutional anomaly, and long before a bacillus was suspected, eminent clinicians had arrived at the same opinion upon this point. Thus, Laënnec says: "It is certain that individuals so constituted form only a small proportion of all consumptives, and that the disease frequently attacks the most robust and shapely individuals." The same opinion is voiced by Louis, Fournet, Hérard, Cornil and Hanot, Germain Sée, and de Renzi. Villemin also repudiates the notion that the so-called habitus is a predisposing factor, and says, by way of accounting for the idea, that pulmonary consumption was previously recognized only after profound disorganization had secondarily effected changes in the individual.

We may admit that the paralytic form of thorax is a sign of weakness, and that feeble individuals, with weak ciliary epithelium, are perhaps less fitted to withstand the onset of the disease, and we may from these admissions construe some sort of a causal relation between tuberculosis and the so-called habitus. But, even so, that oft-repeated assertion that people with the habitus phthisicus contribute a greater proportion of victims than others is still unproved. Indeed, the experience of a large number of clinicians, from Laënnec to our own day, is against this assertion. A correct estimate might be gained only by also taking account of the increased danger of infection through the family, which the greater number of such individuals owe to their descent from tuberculous parents.

In so far as regards the purely theoretical interest of the problem, it certainly has little importance. But it may assume a very practical aspect for the patient, in case his physician hesitates to diagnose phthisis in the face of an excellent constitution and a well-developed thorax, and so wastes the most valuable time for treatment.

[Woods Hutchinson* claims that the view that the phthisical chest is flattened from before backward is incorrect. He holds that this appearance is produced by the bowing forward of the shoulders, but says that on measurement the chest of phthisis is really elongated cylindrically. Colbeck,† of Victoria Park Hospital, London, confirmed Hutchinson's observations. From his observations he deduces the interesting explanation that the phthisical chest is a persistence of the infantile type, and suggests that susceptibility to phthisis is due to this fact. Further investigation of this interesting point is needed before the question can be permanently settled.—Ed.]

When the disease has reached a certain grade, inspection reveals a diminished excursion of the diseased area of the chest with deep inspirations and, perhaps, even a certain immobility. This is most marked at the apex and over the upper ribs, corresponding to the favorite site of localization of the process. It is of importance, in eliciting this sign, not to permit the patient to raise the shoulder girdle or render his muscles tense. Contraction of the lung may give rise to circumscribed areas of retraction, particularly in the upper portions of the thorax. These are not to be confused with the deepening of the infraclavicular hollow, due to unilateral or symmetrical absence of the upper fibers of the pectoralis major, as described by Hyrtl, von Ziemssen, Bäumler, von Noorden, Riegel, and others. Extensive areas of retraction are, as a rule, attributable to the absorption of pleuritic exudates.

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* Brit. Med. Jour., Oct. 28, 1900.

† Jour. Amer. Med. Assoc., May 2, 1903.

THORACOMETRY.

The shape of the thorax becomes altered by the tuberculous process only after the disease is far advanced, when cavity formation and contraction have taken place. The area of chest-wall overlying the focus of disease then becomes retracted and sunken. Such alterations are, as might be expected, most frequent over the apices, which are in general the oldest foci.

Vicarious emphysema, and especially exudative pleurisy, may secondarily compensate for considerable contracture, and may even outbalance it, so that inspection fails to discover any defect.

PALPATION.

Palpation generally confirms certain conclusions suggested by inspection, namely, the deformity of the thorax and the loss of muscular tone. If both hands be placed on the thorax, the diminution of motion on the affected side becomes even more evident than by inspection.

Further, the diseased side offers increased resistance to the palpating finger, simply by virtue of the pulmonary infiltration. This is, of course, very much enhanced if an inflammatory process has been set up in the costal cartilages with premature ossification.

Palpation also reveals an increase of fremitus when the patient is told to speak loudly. An increase of this kind is brought about by the removal of those factors which tend normally to obstruct the transmission of the sound-waves, namely, the numerous reflections to which these waves are subjected in passing from the air of the alveoli to their walls, and so on. More favorable conditions for the transmission of sound are furnished by the presence of homogeneous solid masses, of atelectatic areas of lung (cheesy tracts, fibrous cicatrices, pneumonic consolidations), or of superficial, firm-walled cavities. To appreciate this phenomenon properly, one must remember that vocal fremitus is always greater over the right half of the thorax than the left, on account of the greater diameter of the right bronchus. The important element is the difference between symmetrical areas on the two sides of the chest. In order to become evident by means of palpation, the altered areas must lie not too far removed from the surface of the lung; the increased vocal fremitus which they occasion may again become damped by the interposition of areas of healthy tissue. Vocal fremitus is especially well marked when tense pleuritic adhesions unite the lung with the chest-wall. On the other hand, pleuritic exudates, pneumothorax, and occlusion of the bronchi tend to diminish the fremitus. Infiltration of the anterior margin of the left upper lobe permits one to feel the closure of the semilunar valves in the pulmonary artery.

The more the process advances, the more marked do these phenomena become.

PERCUSSION.

Percussion yields valuable information concerning the position and the extent of tuberculous areas in the lung. In the earlier stages of the disease it does not, indeed, help very materially. The diminution in the respiratory area which is brought about by the growth of the tubercles and by the deposition of the products of their disintegration in the neighboring bronchioles, is not sufficient to alter the percussion note. The effect of these small areas of consolidation upon the note is more than counterbalanced by the resonance of the surrounding healthy portions of lung tissue.

In general, areas at the surface must have attained an extent of 4 to 6 cm., and a depth of 2 cm., before they are capable of altering the pulmonary resonance. Flatness is produced only by foci of a depth of at least 5 cm. Smaller foci, and such as lie deeper than 5 cm.,—for example, central caseous foci and tuberculo-pneumonic areas,—may entirely escape observation (Piorry, Friedreich, Eichhorst).

Inasmuch as the individual tubercle requires two or three weeks for development, it is easily seen that a considerable time, perhaps months, must elapse before a tubercular focus can attain anything like the size necessary to become manifest through percussion. This holds true even of the apices, in which the vibrating mass is of limited extent, and in which pathological areas even smaller than the minimal size, as stated above, are at times discoverable. This circumstance tends to diminish the diagnostic value of percussion. Before speaking of the various alterations in resonance which occur during the course of phthisis, it may be well to recapitulate the fundamental principles of our knowledge of percussion (see pages 422–425).

As the immediate consequence of the tuberculous process is a limitation of the air-content of the lung, it follows that the first physical evidence of its presence will consist in a shortening, a weakening, and a decrease of the normal full and sonorous pulmonary resonance. As the consolidation progresses the dulness continually increases, and gradually becomes absolute ("thigh-note"). When multiple small foci compress the intervening tissue and render it tense, there is tympany.

During percussion the muscles of the chest and shoulders should be relaxed, the chest should not be protruded, the head should be held erect and in the median line. Light percussion elicits the character of the superficial strata; heavy percussion, that of the deeper parts.

As the apices are generally the seat of the earliest development of the tubercular process, so they are also the usual site of the earliest dulness; thus, in 104 consumptives Grawitz found that the process had originated in the apices in 88 per cent.

The dulness is not at first sufficiently marked itself to attract attention, although it becomes unmistakable when compared with other areas.

Even the normal percussion note varies not only with the character and the extent of the vibrating portion of the lung, but also with the resonance of the thoracic wall, and with the thickness of the muscular and fatty layers. It has been very properly said that every person has his own note, and that that of a child, for example, with its flexible bones and cartilages, is very different from that of the old man, with atrophy of the muscles and the fat. For the same reasons, the percussion note varies over different parts of the same chest. The maximum of resonance is obtained in the intercostal spaces, especially the two upper ones, below which it diminishes in intensity. Resonance decreases from the sternum toward the axilla (presence of muscle). It is also diminished in the supraclavicular spaces (diminished pulmonary tissue), being there greater externally than internally. It becomes still weaker over the clavicle; in the supraspinous and infraspinous fossæ it is very weak on account of the dense muscular layers.

QUALITY OF NOTE.	PHYSICAL CONDITION OF PERCUSSED AREA.	PHYSIOLOGICAL AND PATHOLOGICAL OCCURRENCE.	REMARKS.
I. **Flatness,** slight intensity.	Absence of air (consolidation or fluid).		As if percussing the thigh.
II. **Resonant,** loud	Containing air,	Pathological: Innumerable variations according to the degree of the process from a loud or tympanitic note to one of slight intensity or even flatness (complete absence of air).	
it is more resonant	the larger the area		
it is duller	the smaller the area.		
(1) **Non-tympanitic**	With high tension of walls (without regular vibrations)	When the alveoli and bronchi are filled with material containing no air (fibrinous or cheesy pneumonia), tumors, or airless fluid (edema, blood).	Vocal fremitus increased.
(α) It is of slighter intensity and duller	the greater the tension of the chest-wall and lung		
	the smaller the vibrating area.		
High and low pitch hard to differentiate		When the air is forced out of the alveoli by pressure (of neighboring structures, pericardium, abdomen); when there is no air in the alveoli from collapse or obliteration.	
		When there is a solid or fluid between the lung and the chest-wall, pleuritic exudate, tumors of the pleura.	Vocal fremitus diminished.
		When there is a collection of gas in the pleural cavity under high pressure: Pneumothorax.	Diseases of the bronchi in themselves do not change the percussion note.
(β) It is loud, clear, full, resonant	If the chest-wall and the pulmonary tissue are not under tension and if the vibrating mass is large.	Physiological: normal lung in the chest.	
(γ) Strikingly full and clear	When the elasticity is diminished.	Pathological: Emphysema.	
(2) **Tympanitic** (metallic quality)	When there is no tension in wall (comparatively regular vibrations)	Physiological: Stomach, intestines, larynx, trachea.	
The pitch is higher	If the cavity is small, if the column of air is short,	Pathological (*a*) Cavities (tuberculosis, gangrene, abscess, bronchiectasis).	Differential diagnosis by sputum, development of symptoms and other evidence of disease.

Quality of Note.	Physical Condition of Percussed Area.	Physiological and Pathological Occurrence.	Remarks.
The pitch is higher	if the orifice is large, if the tension of the wall is moderately high, if the vibrating mass is small.	(*b*) Relaxed lung tissue from (*a*) diseases of alveoli when air and fluid vibrate at the same time (edema, hemorrhagic infarcts, bronchopneumonia, first and third stages of fibrinous pneumonia.	Cavities size of hazelnut are demonstrable if they are superficial, smooth-walled, surrounded by consolidation and have a large orifice; otherwise only if size of walnut. Dull tympany over pneumonic consolidation.
The pitch is lower	If the cavity is large, if the column of air is long, if the orifice is small, if the tension of the wall is low, if the vibrating mass is large.	(β) Diseases of the bronchi, plugging with mucus, pus, blood, fibrinous exudate, foreign bodies. (γ) Disease of neighboring organs, pleura (large and moderate sized exudates), pericardium (pericarditis, great hypertrophy).	Small inflammatory areas of lobular distribution and tumor masses compress the aërated tissue that lies between.
		(*c*) Sometimes in open pneumothorax.	Dulness in closed pneumothorax on account of excessive tension. If it is a hydro- or pyo-pneumothorax the tympany is usually higher when patient is erect because fluid depresses the diaphragm and increases the vertical diameter; Biermer's change of note: with small amount of fluid —vice versa.
		Signs of cavity (to differentiate from relaxed lung): (*a*) Change of percussion note. The tympany is replaced by a dull note or one of slight intensity if both air and fluid are present, and especially if the latter is thin and considerable in amount (most marked with gangrene, abscess). (*b*) Respiratory change of note (Friedreich). On inspiration the tympanitic note becomes higher and may even disappear if tension of wall is very great. (*c*) Wintrich's change of note. The tympanitic note becomes higher when mouth is open (latter acts as resonator and increases the tones corresponding to its own tones), lower when mouth is shut. When the orifice (bronchus) is plugged there is no change of note; this can be produced after coughing.	

QUALITY OF NOTE.	PHYSICAL CONDITION OF PERCUSSED AREA.	PHYSIOLOGICAL AND PATHOLOGICAL OCCURRENCE.	REMARKS.
		(*d*) Gerhardt's change of note. If the position is changed, the head being held in same position, when the contents are movable (air and fluid) the note becomes higher and lower according to the direction of the longest diameter of the cavity (only indicates cavities when the erect position raises the pitch).	
III. **Amphoric,** bell-like (independent of tympany).	The high tones predominate in cavities with smooth walls, on account of the regular reflection of sound-waves from the walls.	(*a*) Cavities with smooth, firm walls or even with a solid cheesy coating when situation is sufficiently superficial and size sufficiently large.	Disappears at times when the inner surface becomes uneven from blood, pus, or cheesy masses. Heard with difficulty when the bronchus leading to it is plugged.
	More distinct over open cavities than closed; more distinct when mouth is open.		The longest diameter, according to Wintrich, must be at least 6 cm. in diameter. According to Skoda, demonstrable when size of fist, sometimes even when 3.5 cm. in diameter.
	Is more distinct the smoother and more firm the wall, the more superficial the situation, the wider the orifice, the nearer a main bronchus for conduction of sound.	Pneumothorax, often heard with difficulty because the cavity is closed on all sides; is absent when tension of air is excessive.	If the pneumothorax contain fluid also (pyopneumothorax), the amphoric note shows Biermer's change of note.
	More distinct by auscultatory percussion, artificial pleximeter percussion (Heubner) or finger pleximeter percussion (Stern).	Very rare in fibrinous pneumonia (Stern, de Renzi) and in pleurisy.	
IV. **Cracked-pot** (bruit de pot fêlé).	Arises by formation of air-waves when air is forced out through a narrow orifice (stenosis murmur). More distinct when mouth is open and stroke is short and firm. Sounds as if the knee were struck with hollowed hands.	Physiological: Present in percussion of adults and especially of children when crying, speaking, singing; sometimes audible when the pleximeter is held loosely or is applied to a very hairy, dry chest. Pathological: In cavities communicating by a narrow orifice with an open bron-	Not a dead sound, as Cotton says. The chief point of origin of this sound, if a cavity is present, is at the opening into a bronchus, provided this is large and the usual conditions in the larynx prevail.

Quality of Note.	Physical Condition of Percussed Area.	Physiological and Pathological Occurrence.	Remarks.
		chus. Most commonly in tuberculosis cavities in apices (rarely bronchiectasis because they are covered by aërated tissue). More rarely over relaxed or infiltrated or tuberculous lung, pleuritic exudate, or in open pneumothorax (communicating externally or with a bronchus).	

An accurate appreciation of the real value of the percussion note as found over any given portion of the thorax is obtainable only through comparison with that of the symmetrically opposite area, at least so far as local differences, such as the heart on the left side, do not invalidate this symmetry. It must also not be forgotten that the musculature of the right half of the thorax, especially the pectoralis major, is often far better developed than that of the left half, and that the note may thus be rendered considerably flatter. This is observed particularly in laborers.

Slight changes of note are first appreciated by comparison with the opposite side. Very minute differences are not available in diagnosis. As an example, I may give an incident of my student days. Two very renowned and experienced physicians exhibited the same patient on the same day, the one in the morning, for dulness of the right apex, the other in the afternoon, for dulness—over the left apex!

Symmetrical slight diminution of the note over both apices is often overlooked. At times it becomes evident only after careful and repeated examination.

Dulness in itself gives no information concerning the nature of the underlying changes. It does not inform us that there is a tuberculous change, but only indicates that the air-content in the deeper planes is subnormal and pathologically diminished. If this change, however, involves the apex, we may conclude with a probability bordering on certainty that the nature of the process is tuberculous, since we know that other affections tend to spare this site, while it is the especial predilection of the tubercle bacillus. Absolute certainty can be attained only by the simultaneous observation of all accompanying symptoms, subjective and objective, auscultatory and by sputum examination.

Of exceptional importance is the determination of the level of the two apices. Normally, the apices in the adult extend 3 to 5 cm. above the clavicles, and almost invariably reach the same height on both sides. In men and in slender persons they reach somewhat higher than in women and stout people. In emphysema the apices extend unusually high, even as much as 6.5 cm. (Weil, Eichhorst). Posteriorly, the apices are on a level with the spine of the vertebra prominens (seventh cervical).

Braune observed a number of healthy individuals in whom the apices were of unequal height. This, however, is such a rare event that E. Seitz and later von Ziemssen have ascribed pathognomonic importance to asymmetry of the apices either anteriorly or posteriorly. If in percussing from above downward (v. Ziemssen) we find that the apex does not reach as high up as normally, we are entitled to assume either infiltration or a cicatricial contraction. Auscultation alone can inform us as to whether the condition represents an old quiescent lesion or a fresh and progressive affection. Krönig considers the determination of the lateral extent of the apices to be of importance. He found that it could be indicated by a line drawn from the middle of the anterior border of the trapezius in the supraclavicular space, running downward in a rather steep curve, cutting the clavicle at the junction of the middle and outer thirds, and then prolonged obliquely outward toward the axilla.

In certain cases of healthy persons, in whom there was a depression of the apex, like that found in cicatrization of the lung, he found that there was also a decrease in the lateral extent of the apex.

A diagnostic pitfall which must often be reckoned with may here be mentioned. Diminished resonance over the apices may also be due to a previous apical pleurisy, which dulls the note in the same manner as do the fatty and muscular layers. Vicarious emphysema may follow upon contraction, and may serve to obscure the flatness and the surface depression. An emphysematous apex may even have an increase of resonance, and thus betray the physician into the error of regarding the resonance of the healthy side, which is relatively reduced, as pathologically diminished. Finally, one must keep in mind the possibility of modifications in the note by means of glands, mediastinal tumors, and aneurysms. Absence of dulness does not indicate absence of disease, inasmuch as a focus alters the resonance only when it has attained a certain size. Large numbers of disseminated tubercles or numerous smaller pneumonic foci may entirely escape detection by means of percussion. Whenever I find a case in which the general symptoms of tuberculosis are present, and in which percussion is nevertheless normal, I always have an uncomfortable suspicion that there may be multiple foci of small extent.

As has been said, changes of note are ordinarily most evident at the apices in the early stages. There are exceptions, as when the primary focus is situated behind the second rib, or in the postero-inferior portions of the lung. Examination of the apices alone might easily lead to gross errors in diagnosis. As the process advances, the dulness spreads beyond the first rib anteriorly to the middle of the scapula behind, and finally passes over to the opposite side.

As a rule, tuberculous dulness is not absolute, inasmuch as the lesions do not involve whole patches of lung, as in pneumonia. The most marked dulness accompanies the cirrhotic processes.

The mode of development of phthisis is of such a kind that there is no continuous advance either of the disease itself or of the physical signs. The changes occur by leaps and bounds. Some lobule of lung, large or small, relatively near to the primary focus, or far removed from it, becomes suddenly inundated through the aspiration of tuberculous secretions. A pneumonic focus forms rapidly, under the influence of the proteins or of the secondary bacteria. Such a focus may undergo resolution or may fuse with other similar foci to form a conglomerate tubercle. The latter occurs especially if live bacilli are present. The percussion note evidences only the solidity and the relaxed condition of the alveoli; it gives no clue as to the nature of the process, whether it is an eruption of tubercles, or a protein pneumonia, or a secondary pneumonia. The activity of the process provides a useful hint, inasmuch as tubercle formation is a very slow affair. The further progress of the disease is marked by softening and caseation in the older foci. Cavities are formed, and the signs above described gradually become evident, namely, tympany, metallic resonance, *bruit de pot fêlé*, and changes of note.

The conditions become still further confused by the frequent occurrence of a vicarious emphysema by pleuritic exudates and by the numerous varieties of pneumothorax. Often the phenomena become jumbled together in inconceivable abundance and confusion; there are innumerable gradations between tympanitic and non-tympanitic areas, and such as are absolutely flat.

Of the changes found in the other organs, that which is produced by enlargement of the liver is especially noteworthy. It occurs in the later stages (Gerhardt). The organ may be soft, yielding, smooth and flat (fatty liver); or hard (amyloid), with simultaneous enlargement of the spleen. At times there is an increase in the area of cardiac dulness.

AUSCULTATION.

Of very great importance are the changes which occur in the auscultatory phenomena, being secondary, indeed, only to the findings in the sputum. Here, too, we may preface a brief sketch of the phenomena, their physical basis and pathological significance (see page 429). We have no signs which are pathognomonic of tuberculosis. Nevertheless the fact that tuberculosis in the vast majority of cases first attacks the apices is of great assistance. Other diseases also involve the apices, but are never entirely limited to them. Therefore changes in the breathing over these portions of the lung alone should invariably arouse suspicion of the disease.

At first, and as long as there are only isolated and separate tubercles, there will be no auscultatory variation. The predominance of the normal vesicular breathing masks all abnormalities. Even well advanced miliary tuberculosis does not at first alter the vesicular character of the breathing, or only slightly intensifies it.

Only when the tubercles have invaded a large number of alveoli and bronchioles, in other words, only months after the primary infection, are we able to detect any changes by auscultation.

The process is most diversified in character, and consequently presents no single form of "primary signs." The signs vary with the nature of the changes in the lung, as the following examples may illustrate. The disorganized detritus in one set of cases is rapidly thrown off in the sputum; in others, masses of it clog the bronchioles, irritate them, and produce mucous catarrh. The signs are very characteristic when a large number of tubercles lie at the surface of the lung and irritate the opposite pleura; they differ immensely, however, when the tubercles spread rapidly through the lungs by means of the lymph courses.

CHARACTER.	PHYSICAL CONDITION.	PHYSIOLOGICAL AND PATHOLOGICAL OCCURRENCE.	REMARKS.
Vesicular breathing (breezy).	Heard usually only in inspiration; when heard in expiration has more of an indefinite, blowing character. It is formed as bronchial breathing from the air-waves that arise beneath the vocal cords (narrowing) and is a stenosis murmur. Transmitted downward and transformed by the vibrations of the tense pulmonary tissue (bronchioles and alveoli) into vesicular breathing (Penzoldt's experiments); is therefore dependent upon the content of air. In expiration the stenosis murmur is formed above the vocal cords. Transmission downward is therefore difficult on account of the opposite direction of the expired air.	Heard normally over healthy lung.	It is of higher pitch in children and women (narrower larynx) than in men. Higher in old age (rarification of lung tissue).
Feebler.	If the breathing is slow and superficial, if the passage of air is slow, if the chest-wall is thick (therefore feebler over the female breast and over the back).	Pathological: Plugging of bronchi (swelling of mucous membrane, foreign bodies). Compression by small amount of fluid or air in the pleura and by tumors. Change in thickness of chest-wall (edema, tumors). Diminished respiratory movements (on account of pain; pleurisy, muscular rheumatism; adhesions, alveolar emphysema).	
Exaggerated, harsh, coarse.	From increase in rapidity and depth of the respiratory movements.	Nervousness, hysteria, dyspnea vicarious if the activity of one side is prevented. Obstruction in the bronchi (secretion, swelling).	

CHARACTER.	PHYSICAL CONDITION.	PHYSIOLOGICAL AND PATHOLOGICAL OCCURRENCE.	REMARKS.
Cog-wheel breathing.		In painful affections of the pleuræ and thorax, when there is swelling of the medium-sized and small bronchi (uneven entrance of air, often harsh in addition).	Often in excited children.
Vesicular inspiration and prolonged expiration.		Obstruction in the mucous membrane of the bronchi, bronchitis (at the same time often harsh and cog-wheeled). Asthma and alveolar emphysema.	
Bronchial breathing (blowing).	Physiological: Larynx, trachea—often, though weak, can be heard in interscapular region (more commonly on right side than on left), owing to situation of bifurcation of bronchi; less commonly in the supraspinous, supraclavicular, and infraclavicular regions over the spine as far as the fourth cervical vertebra. Is louder in expiration, because in expiration, the glottis being narrow, the formation of air-waves is more marked.	Pathological: Though present with quiet breathing, it is loud and well transmitted: (1) If a large superficial area is void of air and encloses a large bronchus. Pneumonia, tuberculosis, gangrene, tumor, rarely when full of airless fluid, obliteration, contraction, compression, from diseases of pleura (moderate sized and large exudates, air, tumor), from cardiac complications (pericarditis, hypertrophy), from abdominal complications (ascites, peritonitis, meteorism, tumor). (2) If large bronchi open into superficial cavities with solid walls owing to the air vibrations caused there.	Commonly heard where there is a tympanitic percussion note and exhibits similar characteristics (when mouth is open).
Changeable breathing (metamorphosirendes Athmen).*		Important diagnostic sign of cavity, rare in fibrinous pneumonia.	(Kotowtschikoff, Eichhorst).

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* For the German "metamorphosirendes Athmen" we have no exact English equivalent. By it is understood breathing, usually of a bronchial character, that differs in character or pitch or both in inspiration and expiration. The commonest form is a change from a loud blowing bronchial inspiration to a much softer bronchial or even amphoric expiration.—ED.

Character.	Physical Condition.	Physiological and Pathological Occurrence.	Remarks.
Amphoric breathing of metallic quality.		Often accompanies metallic percussion note (loc. cit.) and is of a like diagnostic significance (large cavities and open pneumothorax and pyopneumothorax), rarely in the neighborhood of a tense hollow organ (stomach), exceptionally in dyspnea, in pleuritic exudates in old people (interscapular).	
Broncho-vesicular breathing.	In slow, superficial breathing when transmitted through thick fluid or solid masses.	When bronchi are plugged with secretion or compressed in the case of exudates, infiltrations and tumors.	
Dry rhonchi.	Viscid secretion, catarrhal swelling, narrowed lumen (stenosis murmur, air vibrations formed on the other side of the obstruction).		Of no value for diagnosis of tuberculosis only in concomitant emphysema and asthma.
Sonorous, purring.	Majority in the larger bronchi.	Central rhonchi hidden in spite of much sputum.	
Sibilant, whistling, hissing.	In the smaller bronchi.		
Moist rhonchi.	In bronchi, alveoli, and cavities.		Dry rhonchi only in bronchi.
Numbers depend on amount of secretion.	Only when secretion is fluid.		
Large, medium, and small sized râles.	Those in terminal bronchi and alveoli only small sized.		
Small sized, crepitant, vesicular râles.	When alveoli and the smallest bronchi are partially filled with exudate. Heard almost entirely with inspiration, from the separation of the alveolar walls from the viscid secretion.	First and third stages of fibrinous pneumonia, edema of lungs, hemorrhagic infarcts, capillary bronchitis.	Almost entirely in the second half or toward the end of inspiration when the air has reached the alveoli; sometimes it disappears after a few deep respiratory movements and reappears again later.

CHARACTER.	PHYSICAL CONDITION.	PHYSIOLOGICAL AND PATHOLOGICAL OCCURRENCE.	REMARKS.
Ringing, consonating râles (never of the smallest size, as the alveoli must be void of air).	In bronchi surrounded by airless lung pulmonary tissue or which empty into superficial, firm-walled cavities (Better conduction.) The cavity may be an encapsulated space in the pleura.	In pneumonic, atelectatic, and tuberculous infiltrations as well as over cavities of moderate size.	Almost always accompanied by bronchial breathing and often by a dull or tympanitic percussion note.
Râles of metallic character.	Under same conditions as bronchial breathing of metallic character and metallic percussion note.	Not only inside of cavities, but also in the neighborhood of smooth-walled cavities (pneumothorax, intestine).	
Gutta cadens.	A few bursting, bubbling râles of particularly metallic character.	As above.	

So-called cog-wheel respiration at the apex is often considered a characteristic early symptom. It depends upon the presence of a certain obstruction to breathing, which is rhythmically overcome by the effort. The obstruction may lie in the small bronchi, but is often traceable to superficial tubercle formation, with nodules in the pleura and friction sounds (Colin, Hérard, Cornil and Hanot). Occasionally healthy individuals present this type of breathing, or the inspiratory murmur becomes harsh, loses its coughing character, and gets to be rough and indefinite. The presence of a noticeable diminution of the respiratory murmur upon one side argues for the exclusion of a fairly large area; that is to say, it indicates an extensive tuberculous focus and a well-advanced process. Occasionally the same symptom is temporarily produced through the occlusion of a bronchial radicle.

The above described signs are sufficient in themselves to warrant a suspicion of tuberculosis. The more marked they are, the greater does this probability become. If only one of the apices shows changes, —and a comparison of symmetrical areas, including the apices, is a necessary part of every examination,—and if the findings are confirmed upon repeated examination, the probability approaches a certainty. Taken with other symptoms (emaciation, etc.), a positive diagnosis is permissible.

Whereas normally the inspiratory murmur markedly exceeds the expiratory both in intensity and in duration, in tuberculosis the expiratory phase becomes lengthened, and assumes a harsher and more bronchial character. At times even in healthy people there is a slight transmission of the rough breathing of the trachea and bronchi. But whenever the expiratory murmur approaches or exceeds the inspiratory in duration and in intensity, and whenever it becomes rough and harsh, there is good ground for assuming a catarrh of the mucous membrane, and, if in the apex, a tuberculous process.

As the disease progresses, and extensive areas become infiltrated and caseous, the respiratory murmur completely loses its vesicular character and becomes out-and-out bronchial. The same thing occasionally happens in healthy individuals, but does not attain the same grade. In health, it is found especially in the interscapular region.

The most important part is played by the râles, which are occasionally present before there is any change in the respiration. If râles are constantly found, even though in limited numbers, over one of the apices and at a fixed position, there can be scarcely a doubt of the diagnosis of tuberculous catarrh of that apex.

In some cases the râles appear only upon forced breathing and coughing. One should never neglect, therefore, to explore the patient during and after coughing. At times the râles disappear after coughing, owing to the removal of the mucus; and as the latter collects, they reappear.

Slight crepitation may sometimes be elicited in healthy persons when the lungs are suddenly forcibly expanded, as in taking the erect position after prolonged dorsal decubitus. It results from the rapid opening up of collapsed alveoli and bronchioles, and is found generally behind and below. The phenomenon disappears with a few deep breaths.

Still easier is the differentiation between true tuberculous râles and those due to forcible contraction of the chest muscles—muscular râles (Rosenbach). The latter are more like friction sounds, and occur symmetrically. They are often found over the upper portions of the lung. Confusion with the pseudo-râles due to the beard of the physician or to the clothes is, of course, avoidable.

In the early stages the râles come from the alveoli and the finest bronchi. They are generally crepitant, small, few in number, and tend to recur after coughing. Later they become larger, bell-like, and musical, a sign that the alveoli and smallest bronchi over a fairly large area are involved, or that these are small superficial cavities.

Or, there are isolated, clear, large râles, of a crackling or snapping character. When these are located in the apices, they ordinarily denote the formation of small cavities; when they occur in areas related to the large bronchi, however, they may simply denote the presence of a viscous fluid. They have been called "tuberculous râles."

It is only in the late stages that the metallic note is superadded to bronchial breathing, to the râles, and to the bronchophony. As has been said in connection with percussion, this tone occurs in the presence of large cavities, say 4 cm. in size, with smooth walls and containing air, which permit of a general reflection of the sound-waves. Hence it is most common in cavities. The same significance attaches to the amphoric note in bronchial breathing. Metamorphosing respirations (metamorphosirendes Athmen) (Seitz), a hissing sound during the first third of inspiration, speaks almost invariably for cavities.

Emphysematous and asthmatic patients require a most careful examination to lay bare a beginning tuberculosis. The whistling râles and the orchestral-like music over the entire chest often completely obscure the slowly growing focus in the apex. Recently I had the chance to see three such cases in rapid succession, the first being extremely characteristic. An official of high rank had suffered for years from severe asthma, emphysema, and bronchitis. The physical signs were characteristic of this condition. At the second examination it seemed to me that the catarrhal signs at the apex were rather marked. Investigation of the sputum revealed actually pure cultures of the tubercle bacillus. This patient, as likewise the other two, who also had tubercle bacilli in the sputum, had passed as an uncomplicated case of asthma.

Vocal resonance, the sound perceived by the ear when applied to the chest while the patient speaks, when he says "ninety-nine," for example, gives results comparable to the variations in vocal fremitus. Over pulmonary infiltration, over caseous or other deposits, over cavities with thick walls, in case they do not lie too deep, there is increased resonance. On the other hand, occlusion or compression of the bronchi, as by pleuritic exudates or hydrothorax, results in a diminution or an abolition of the vocal resonance.

Egophony (bleating) may occur, as Skoda showed, above middle-sized cavities and atelectatic areas of lung, also with pleuritic exudates and hydrothorax.

Complicating pleurisies often give rise to friction sounds, which are usually intensified by pressure in the intercostal spaces, but may be obscured by râles. These sounds may be fairly limited in distribution or may cover a wide area of the chest. They indicate either tubercle formation at the surface of the lung or a fibrinous pleurisy. Further consideration of this phenomenon and of the signs of pleuritic exudates cannot be entered into at this place. We may also mention the signs of pneumothorax, which may be deduced from the foregoing sketch.

Von Friedreich, Rühle, and certain English physicians have called attention to a blowing, systolic murmur in the subclavian artery of the diseased side. It shows a certain relation to the respiratory phases, and is ascribed to the traction of adhesions between the pleura and the artery. The phenomenon is not constantly found in consumptives and may be present in others.

Finally, mention may be made of the diffuse and increased pulsation of the heart, and the intensification of the second pulmonary sound.

TRANSILLUMINATION.

Almost from the moment of their discovery the Röntgen rays were drafted into service. Researches upon their value in the diagnosis of pulmonary disease have been made by Bouchard, Benedikt, G. Rosenfeld, Grunmach, Levy-Dorn, Büttner, K. Müller, and others. The latter have denominated the new method "pyknoscopy"; Rosenfeld has called it bioscopy. I assume that the arrangement of the apparatus is understood. Von Ziemssen praises highly a newly discovered flexible shield of platinum cyanide, which I have not, however, been in a position to test.

The work which has as yet been done does not entitle us to give a final estimate concerning the method. There is certainly good ground for hope that transillumination will develop into a valuable aid in diagnosis. The present status of the subject is as follows:

The normal lung throws no shadow. The bones of the thorax and the pulsating heart appear on the screen as distinct shadows, but the lung area shows up bright and clear to the very tips of the apices. Infiltrations of lung and pleura (phthisis, calcareous foci, pneumonia, gangrene, tumors, cicatrices, and effusions) throw shadows. It is to be observed that there may be areas of more or less opacity in the normal lung, particularly at the apex and at the inner border of the shoulder-blade, occasioned by increased thickness of the muscles. Raising and depressing the arm and the shoulder shows whether the opacities are caused by the muscle or by pulmonary lesions (Rosenfeld). Bouchard and Benedikt have detected shadows in apical disease. Further, Büttner and Müller, Williams, Claude, Beclère, the author, and others have confirmed the diagnostic value of transillumination of the lungs, especially of the apices, in the diagnosis of tuberculosis.

In a consumptive who was to all clinical appearances cured, I was able to determine shadows of considerable extent in the diseased areas.

Wassermann diagnosed a cavity near the anterior chest-wall, which could not be demonstrated by percussion; by means of a skiagram it appeared as a light spot in the dark area of infiltrated lung. As Rosenfeld rightly observes, the diagnosis of phthisis by means of the *x*-rays requires very great experience, inasmuch as there are some phthisical foci which give a definite shadow, while others give none at all.

[During the past four years the Röntgen rays have not realized all that was expected of them as an aid to the diagnosis of early pulmonary tuberculosis. Williams* finds a noticeable limitation of the excursions of the diaphragm on the affected side, even in mild pulmonary tuberculosis,—an observation which had been previously made by others,—and he considers this an important point in the recognition of the earliest stage of the disease. He has also noticed a displacement of the heart toward the affected side, explained by the over-strong push of the diaphragm on the healthy side and by the pulling of the adherent pleura as well.

Capo† confirms this observation of Williams, and claims that radioscopy reveals also the small size of the heart in advanced phthisis.

Brook and Green‡ find the *x*-rays useful in diagnosis and in watching the progress of the disease. They say that the only fallacies are caused by chalk deposits in the lungs, by old healed cavities, and by thickened pleura.

Further observation confirms the impression that radioscopy and radiography have but a limited field in the diagnosis of pulmonary tuberculosis. In the hands of an expert they are at times of considerable service, but they require a degree of technical skill and an amount of experience that render them of little practical value to most practitioners, and in the hands of others than experts they are more apt to mislead than to aid.—Ed.]

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* The Röntgen Rays in Medicine and Surgery, New York, 1903.

† Medical Press and Circular, Nov. 27, 1901.

‡ Eng. Quart. Med. Jour., Aug., 1903.

SPIROMETRY.

Pulmonary tuberculosis results in a diminution of the "vital capacity" of the lungs, by which is meant that amount of air which is expelled by the most forcible possible expiration following the deepest possible inspiration. It may be measured by Hutchinson's spirometer, or any properly constructed gasometer, or Waldenburg's pneumatic apparatus.

Even under normal conditions the vital capacity of different individuals varies in proportion to the respiratory area and the size of the lung. The attempt has been made to establish a measure by which the normal vital capacity in each case could be determined. According to Hutchinson, vital capacity increases with the height of the individual. He determined that the increase was 131 cc. for every 2.5 cm. of height over 150 cm. Fabius based his calculations upon an estimate of the capacity of the thorax regarded as a cylinder, of which the dimensions could be ascertained by measuring the length of the trunk, the circumference of the thorax, and the mobility of the chest. Simon, Schneevogt, Wintrich, Arnold, Faivre, Müller, Waldenburg, and others have attempted to determine a normal standard. According to Wintrich, to every centimeter of height there is of vital capacity—

	Both Sexes.	
	cc.	cc.
Between ages of 6 and 8	6.5	9
“ “ 8 “ 10	9	11
“ “ 10 “ 12	11	13
“ “ 12 “ 14	13	15
“ “ 15 “ 20 few observations.		
	In Men.	In Women.
“ “ 20 “ 40	22–24	16–17.5
“ “ 50 “ 60 great variations.		

For all practical purposes the limits of normal capacity as established by von Ziemssen may be adopted. He found the minimum value in health to be as 1 to 20 in men, and 1 to 17 in women; *i. e.*, 1 cm. of height equals 20 or 17 cc. of vital capacity. These figures have only an approximate value, inasmuch as there are also physiological variations, due to weight, pregnancy, age, chest measurement and chest mobility, gastric contents, etc. Practically, however, they are close enough, inasmuch as the differences due to disease are generally considerable,—10 per cent. or more.

Hutchinson has already observed a diminution of vital capacity in pulmonary tuberculosis. Simon found it markedly diminished in seven cases of miliary tuberculosis. Arnold found a diminution of 12 to 60 per cent. in sixteen persons with a frank tuberculosis. There are similar observations by the above-mentioned authors, also by Hecht, Faivre, Bergeon. If we take von Ziemssen's figures as a basis, a diminution of 1: 18 and lower in men, and of 1: 15 in women, is not rare, even when the signs do not reveal an advanced tuberculous process.

In an advanced stage, when fever, weakness, and destruction of the lung all work together, the relation may sink to 1: 8; in other words, the vital capacity falls to half the normal.

[The consumption of oxygen and the production of CO_2, pulmonary ventilation, have been investigated by Robin and Binet* with interesting results. They find that pulmonary ventilation is markedly increased in 92 per cent. of their cases of pulmonary tuberculosis, the increase being more marked in men than in women. This is contrary to general opinion. They find an increase not only in the amount of oxygen consumed, but in the amount of CO_2 exhaled. This condition they found present not only in advanced pulmonary tuberculosis, but in the very earliest stages of the disease, and present also in all the other forms of tuberculosis investigated, excepting tubercular meningitis, tubercular peritonitis, and lupus. It is present constantly throughout the disease, from the very onset up till death. These observations, if confirmed, will have an important bearing upon diagnosis and treatment.—Ed.]

PNEUMATOMETRY.

There is also a change in the pressure of the inspiratory and of the expiratory blast. This may be measured by the pneumatometer of Waldenburg, essentially a mercury manometer.

According to Eichhorst, the mean values in health are as follows:

	In Men.	In Women.
For inspiratory pressure	44 mm. Hg.	26 mm. Hg.
For expiratory pressure	60 " "	36 " "
And increase in:		
Forced inspiration to	70 mm. Hg.	
Forced expiration to	80 " Hg.	

In consumption the inspiratory pressure is first diminished, later the expiratory; while in emphysema, bronchitis, and asthma the expiratory pressure diminishes, and is often exceeded by the inspiratory (Waldenburg, Hirtz and Brouardel, de Renzi). These values are of no great diagnostic significance in case of slight variation from the norm, but they may serve to gauge the progress of the disease.

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* Acad. de Méd. Paris, March 19, 1901.

In order to avoid the error due to sucking upon the mouthpieces, funnel-shaped mouth-masks are to be preferred to the small tube-like mouthpieces.

CHAPTER III.

COURSES, TERMINATIONS, AND TYPES OF THE DISEASE.

If we briefly recapitulate our previous statements concerning the origin and the dissemination of the tuberculous process in the lungs, we shall better understand the extraordinarily variable picture which pulmonary tuberculosis clinically presents, the diversity of the courses which it pursues, and its terminations, either in death or recovery.

MODE OF DISSEMINATION.

There is a general inclination to dispose briefly of the entire question by assuming a variable degree of innate predisposition on the part of the individual. The organism is pictured as a culture-medium, which is either favorable or unfavorable to the growth of the bacillus, as the case may be. If it is favorable, the micro-organisms multiply rapidly, spread at large, and destroy the individual. In the opposite case the germs of the disease maintain a bare existence, and are eventually overcome by the "organic forces," or whatever one pleases to call them. This is not the place to discourse at length on the various hypotheses and theories upon phagocytosis and the construction of antitoxins and alexins. We are not as yet in a position to estimate properly the rôle which these various elements play in tuberculous disease. Be that as it may, in my own mind there is no doubt that other factors enter very largely into play—factors which concern not the growth of the bacillus, but its dissemination through the lung. This dissemination occurs by continuous growth, *i. e.*, by way of the lymph-channels, by aspiration of the secretions, a type which finds its expression in the widely separated and often extensive pneumonias; and, finally, by way of the blood-stream, which results in miliary tuberculosis of the area controlled by the vessels eroded.

Elsewhere we have explained the individual variations which present themselves, upon the theory that in certain individuals, especially younger ones, resorption goes on more rapidly and the lymphatic channels are more patent; the proteins formed in the tubercles and diffused about them are consequently more rapidly taken up and carried into the blood-stream. The results of this rapidity of absorption are twofold. In the first place, the phenomena of intoxication—fever, emaciation, sweats, anemia—become much more pronounced. In the second place the removal of the toxins from the direct neighborhood of the tubercle opens the door to rapid extension by way of the lymph-spaces (lymphatic dissemination).

In those invalids, however, in whom other conditions maintain, in whom absorption is diminished or the lymphatic channels are less permeable, the proteins tend to remain in the neighborhood of the tubercle. These toxins irritate the tissues, narrow the lymph-spaces, and obliterate the vessels, thus giving rise to the formation of an inflammatory wall which not only prevents the further dissemination of the proteins, but exercises a varying degree of control over the further progress of the bacillus.

It is possible that the activity with which absorption goes on is the essential factor in determining the progress and character of the disease. In all probability the tissues of every individual evince an effort and a capacity to respond by means of a reactive inflammatory process to the stimulus of the tubercle-proteins, if these are only sufficiently irritant in character and are not too rapidly removed. If, on the other hand, the proteins are swept away by the lymph-stream or the lymph-spaces, the stimulus towards the formation of a line of demarcation is lacking.

As has already been shown (see page 379), the absorptive capacity of the individual depends to a certain extent upon his age. Other factors seem also to influence it to a very considerable degree. Thus, nutrition plays an important rôle, inasmuch as the tissues of a well-nourished individual tend to absorb the toxins less readily and less rapidly. Physicians have unconsciously made therapeutic use of this principle, and the good effect of hearty nutrition in tuberculosis is perfectly evident. In emaciated individuals, especially if the loss of weight has been rapid, it seems as though the absorption of proteins, as of the adipose tissues, were greatly facilitated. This may be due to a variety of causes. It is possible that the mechanical easing of the circulation is chiefly instrumental; it is possible, too, that the nutritive fluids of an emaciated individual, being poor in albumins, actually thirst for the proteins and eagerly absorb them, while those of a well-nourished individual have a sufficiency of albumin. In this way we might explain the well-known fact that a pulmonary consumption which was previously mild becomes more severe and more extensive after diseases associated with marked nutritional disturbance, *e. g.*, typhoid, or after insufficient feeding, or as the result of cares and worries, or of other alterations, psychical or physical in kind. These are conditions which demand further investigation, and are also likely to repay it, if only we do not try to unlock every problem with the pass-key "predisposition."

Possibly, too, this affords an explanation of the exacerbation in tuberculous processes following upon pneumonia, since the exudation of the latter disease may, as it were, wash out and destroy the areas of peripheral resistance of those tubercles which lie within its focus. In the same way, traumata may favor the dissemination of the bacilli, if they act upon tuberculous bronchial glands, or upon a focus in the lung previously encapsulated, and especially if they are accompanied by a lesion of the tissues or by a hemorrhage.

Not only the periphery, but the center of a focus is of significance in the dissemination of germs, in case it softens and opens into a bronchus. It depends upon the activity of the ciliated epithelium, upon the localization of the nodule, and upon a variety of other factors, whether the elimination of the secretions is rapid and complete, or progresses so slowly that there is secondary irritation of the bronchi with the formation of fresh foci. Thus a ball of sputum, in its outward passage, may come to lie just before the mouth of a bronchus at the very moment when the individual makes a deep inspiratory effort, as in running, or hurrying upstairs, or coughing; naturally the mass is sucked in, and sets up a series of changes which vary with the amount of sputum, its character, and the force of the aspiratory effort (dissemination through aspiration).

In the upper portions of the bronchus the sputum is quickly cast out by the next succeeding expiratory effort. Deep inspirations, however, carry it downwards to the corresponding alveoli, where there are no ciliated cells to disturb it, and where it sets up a fresh series of processes. The amount of sputum aspirated determines the size of the new focus; its quality determines the pathological changes. If the particle comes from a fresh caseous focus, with large numbers of live tubercle bacilli, the secondary process is characterized chiefly by tubercle-formation, which becomes evident only weeks later. If, however, the sputum comes from an old cavity, with worn-out and impotent bacilli, the field is usurped by pneumonic processes, as described by Fränkel and Troje. If, on the other hand, there are secondary pathogenic colonies (streptococcus, staphylococcus, pyocyaneus, etc.) in the original cavity, as I have a number of times demonstrated, the resulting processes are typical lobar or lobular pneumonias, and pass under the name of relapses. The secondary invasion may involve a different part of the same lobe, or a different lobe of the same lung, or even the opposite lung.

A. Fränkel and Troje have made an especial study of the clinical picture in these pneumonias, in so far as they are not complicated by the presence of secondary bacteria. Often consumptives who have previously given but few symptoms suddenly fall sick, perhaps with a chill; at other times they drag themselves about for weeks.

Examination reveals the presence of a unilateral lobar or lobular hepatization of the posterior (inferior) portion of the lung. The picture often exactly simulates an ordinary croupous pneumonia with bronchial breathing, crepitant râles, and pneumonic sputa. When the course is acute, a differential diagnosis may not be possible.

As a rule, however, the temperature does not fall by crisis, notwithstanding the fact that crepitant râles indicate a resolution of the pneumonia. The temperature subsequently shows irregular variations, even the typus inversus. Dyspnea and cyanosis are often lacking, the face and mucous membranes early become pallid, the expectoration is greenish and contains but few tubercle bacilli. From the very beginning the urine gives the diazo-reaction. The general condition suffers visibly and there is a great loss of vitality. In some cases there is relative cure.

Finally, dissemination in the lung may take place through the rupture of a tubercle into one of the pulmonary arteries (extension to other organs, see page 474), which results in an eruption of miliary tubercles in the area supplied by the artery; if a vein is eroded, there is a general miliary tuberculosis of hematogenous origin.

I shall not describe here the danger of reinfection, or auto-infection, to which the consumptive is exposed through a careless disposal of his own sputum. This subject is discussed in detail in connection with antibacillary prophylaxis.

ACUTE AND CHRONIC COURSES.

Variable as is the course of pulmonary tuberculosis, it is yet possible to distinguish two types (exclusive of the acute miliary form), namely, acute, florid, galloping phthisis, and the chronic form of phthisis. There are cases which belong strictly to either one of these categories, but for the most part the course of the disease in the same individual fluctuates between the two types, and the acute stage alternates with the chronic.

Let us briefly illustrate the acute form of the disease. The patient gives a history of previous good health or of indefinite prodromata. He falls sick with indefinite symptoms of fever, or of a febrile catarrh, or even of an entirely distinct affection, such as a gastritis. In one case I observed a severe pain in the knee, with fever, which did not give the remotest hint of the existence of a tuberculosis. Often there is a history of some preceding circumstance, such as a forced march, a dance, a mountain-climb, a real or imagined "cold," to which the onset is attributed. Within a few days cough sets in, or if previously present it becomes intensified; there is loss of appetite, and a fairly continuous fever of 38° C. (100.4° F.) or over; sweats and, later, chills occur, and the patient becomes visibly emaciated.

On physical examination, the apex presents slight dulness, a decrease of the respiratory murmur, and a few râles; occasionally the dulness attains a surprising extent within a very short time, *i. e.*, down to the second or third rib. The fever rises to 39° C. (102.2° F.) and over. The sweats become profuse, and feelings of chilliness or actual chills precede the rises of temperature. Malnutrition constantly increases, the pulmonary condition extends, and the loss of weight becomes more evident each day. Within one to three and a half months the disease has run its fatal course, with hardly an intermission, with scarcely an intimation of hope.

An acute onset, however, does not invariably presage an acute course. After a few days or weeks the fever may show continually increasing remissions and a continually decreasing height. The patient recovers for a time, only to become the victim of a rapidly recurring attack. On the other hand, the disease may drag out a chronic course for years, or may even completely subside.

The chronic cases present a different picture. There is a prodromal stage, in which the patient may complain chiefly of dyspepsia, or chlorosis, or one of the other symptoms previously mentioned; or the patient may complain for a long time of a slight cough with expectoration, which he attributes to a bronchial or laryngeal catarrh, but which eventually becomes so obstinate as to send him to a physician.

The lungs reveal little; so little, indeed, that the examinations are apt to be made carelessly and infrequently. Moreover, the general condition improves with proper care or with the advent of summer, and slight losses of weight are again made good. The attack is considered past, and the patient goes back to his previous mode of life.

A few weeks or months later the appearance of the patient again becomes worse; his cough returns, an hemoptysis terrifies him, there are febrile disturbances, sweats, and loss of appetite. The physical signs are now so marked that they can no longer be overlooked, and a diagnosis is made of apical catarrh. Proper treatment again induces a period of quiescence.

The phthisis may pass over into the fibrous form or may become completely healed by elimination of the caseous masses and cicatrization; or there may be an irregularly progressive course, varied by periods of improvement. There is an increasing loss of flesh and strength, and the catarrh obstinately grows worse. The succeeding year is marked by a steady deterioration, with frequent changes of symptoms and of physicians. Death comes either suddenly, or ushered in by a shorter or longer period of acute decline or by a bronchopneumonia or hemoptysis.

Happily, there are not a few cases in which, if not too far advanced, proper and prolonged treatment brings a cessation of the process. The gain in strength is permanent, and the convalescence, which is clinically perfect, is also lasting.

Aside from this favorable outcome, the course of chronic phthisis is ordinarily divided into three stages. The first, phthisis incipiens, embraces the period during which the symptoms are only slightly marked, nutrition is good, and the disease is limited to an infiltration of the apex. The second period comprises the process of softening, during which all the symptoms increase in intensity. The third is the stage of cavities, of advanced consumption with hectic fever. So distinct a separation, though theoretically possible, is often not to be made in practice.

COURSE IN CHILDREN.

Pulmonary tuberculosis in children is very different from that in adult life. In the first place, germs inhaled in small numbers often find their way through the uninjured pulmonary epithelium to the bronchial glands, gain a footing here, and then secondarily attack the neighboring portions of lung, at the hilus, so that their very site contrasts with the apical disease of adults. Furthermore, there is a more rapid absorption of proteins, which evidences itself through emaciation, rather than heavy sweats. For this reason there is less of an effort in the way of fibrous organization of the marginal areas, and a greater tendency toward dissemination by way of the lymphatics and blood-channels. For reasons which are rather obscure, hemorrhages are infrequent. The secretions are generally swallowed, not expectorated. Consequently secondary affections of the intestinal tract are common and involve the glands while leaving the mucosa intact, in the same manner as in the lung. On the other hand, as the individual grows older, the channels of absorption become less pervious, and there is an increasing tendency toward fibrous induration and healing.

DURATION.

The duration of the disease is extremely variable, as may be gathered from the preceding remarks. Depending upon the time which is consumed in the development of the individual tubercles, the period of incubation, extending from the moment of infection until the development of the earliest symptoms, may be reckoned as five to six months. Very frequently, however, a year or more elapses before the disease passes out of the latent stage. This does not, of course, include the cases of acute general miliary tuberculosis.

The florid or galloping form runs its course in from about five to twelve weeks from its outbreak. The chronic form, on the other hand, drags out over months, often over a number of years. There are plenty of invalids who can trace back the onset of their lung trouble, ten, fifteen, or even almost thirty years from the time when they had received the first warning, perhaps in the shape of a dangerous hemorrhage. Of course, in such cases it is not certain that the disease has actually continued throughout this entire period. Indeed, it is far more probable that there have been temporary cures and fresh infections, and that the intervals have been occupied by a bronchitis of a simple chronic nature. The anamnesis of the patient is of little value in this connection.

The determination of the average entire length of the course of a case of pulmonary phthisis is of importance not only from a clinical but also from a politico-economical standpoint. This average may be obtained by finding the sum of the number of years of illness in a definite number of consumptives, and then dividing the former figure (the aggregate duration) by the latter (the number of individuals).

It is usually said that phthisis has an average duration of seven years, reckoning from the appearance of the earliest definite symptoms until death. This estimate is based upon the figures collected by Dettweiler. I consider this estimate far too high for the aggregate of consumptives, in view of the large number of cases which pursue an acute course. In answer to a letter of mine, Dettweiler admitted that his views were based upon observations made in the institutions of Görbersdorf and Falkenstein, and that they included adults of all ages. Hence the explanation of these high figures. The inhabitants of an institution, living under fairly favorable hygienic conditions, and including neither children nor the very acute cases, which are hardly apt to seek institutional care, may very well give an average duration of disease of seven years. According to my experience, the figure is even rather low for this set of cases.

Of the population at large, however, about 80 per cent. are free from taxation, *i. e.*, have an income of less than 900 marks ($225); a large number of these are, therefore, unable to observe the precautions of hygiene and of nursing, which phthisis so urgently demands. For the aggregate of the population, then, inclusive of children and of all the acute cases, seven years represents an average which is far too high. I took the trouble to determine the average duration of the disease upon a basis of 800 cases, and found it to lie between two and three years.

TERMINATION.

CURE.

The termination is either by recovery or death. Of the possibility of a cure there can be no doubt. The findings of pathological anatomy, which ordinarily serve only to expose the uselessness of our efforts, give undeniable proof of this fact. Even Laënnec regarded the calcific deposits in the lung as curative efforts. Among those who have been especially active in demonstrating the existence of these healed tuberculous foci, we may mention Cruveilhier, Rogée, Dejerine, Boyer, Bollinger, Staudacher, Massini, Heitler, Stich, Vibert, Müller, Kurlow, Schlenker, Maerks, and others. Their statements regarding the frequency of these foci vary enormously, and range from four to over fifty per cent. These discrepancies are not hard to explain. Certain authors counted in pulmonary cicatrices which were not tuberculous in origin; again, there have been differences in the material, especially from the standpoint of age; finally, there is considerable latitude in the conception of a healed tuberculous focus. To generalize from these figures, as is usually done, and to assert that one-third to one-fourth of all bodies present healed and so-called latent foci of tuberculosis, is unjustifiable. As has already been shown, these data have been collected almost exclusively in pathological institutes, the autopsies comprising those who had died in the hospital and had not been able to afford burial; in other words, the poorest and most exposed class in the community. The data are, however, of value, as evidence that such cures do occur.

When Brehmer attempted to apply these post-mortem findings to practice, and to accomplish an artificial cure by treatment, he met with opposition from every quarter. Since that time, however, the knowledge that tuberculosis is curable has become part of the general property of physicians, even though it is not always sufficiently appreciated to lead to swift and energetic treatment.

The possibility of cure depends upon the extent of the disease and the conditions under which the patient lives. I hope I may be permitted to pass over the various and varying percentages of cure which have been reported, inasmuch as the personal equation and other factors often render the idea of "cure" peculiarly elastic. Not rarely have cases come to me with severe symptoms of the disease, although they had previously been discharged by others as cured. The material, further, has been gathered from such a variety of standpoints, according to the stage of the disease, or to social condition, or other basis, that no comparison of the figures is possible.

It is, of course, improper to speak of a cure in tuberculosis, in the sense of a *restitutio ad integrum,* since there are certain undeniable alterations in the tissues. Nevertheless, a case may be pronounced cured in which the physical signs indicate cessation of the process, and in which the bacilli have been absent from the sputum for so long a time that there can no longer be question of a slow advance, like a glow in the ashes, or even of viability; in other words, according to our present knowledge of their biology, over a period of from two to three years. Increase or decrease of the individual's capacity for work affords no criterion of the degree of cure.

As regards the factors concerned in spontaneous recovery we have above ascribed it primarily to deficient absorption of proteins. Anatomically, the healed foci present themselves either as fibrous cicatrices, which occur especially in the apices, and often contain caseous, chalky, or calcareous material; or as cavities with clean, smooth, generally thickened walls, a dirty gray or white in color, and of the size of a pigeon's egg or over. The bronchial glands which have undergone caseation and calcification also belong in this category.

As long as the content remains partially cheesy, it would seem, according to Kurlow's inoculation experiments, that the cure is not yet absolute.

If we follow the various stages in such a process of cure, we find that the earliest changes occur in the periphery of the tubercle. Here we may identify, in succession, the inflammatory reaction, the occlusion of the lymph-vessels and blood-vessels, the formation of new connective tissue, and, finally, the transformaton into indurated, cicatricial tissue. The content, the true tuberculous material, is at first the same, whether the case is to terminate favorably or the reverse; it goes through the natural stages of its evolution—it caseates. Only secondarily is there a deposition of lime salts.

The wall of inflammatory tissue is more or less perfect according to the character of the tissues. The larger the focus, the greater is the probability that some defect in the barrier will offer egress to the living bacilli, along the course of some large lymph-space or vessel. Thus, in large cavities we often find that a considerable part of the wall shows fibroid induration, while at some little corner the tuberculous process finds a chance to escape and spread. As the disease extends, the more difficult does this fibroid encapsulation become. From the standpoint of dyscrasias, whether one attribute the immunity to the chemical qualities of the serum or to the blood, it is extremely difficult to explain this close juxtaposition of areas of cure and areas of destruction in the very same individual, and often at the very same place.

As long as there continue to be living bacilli in such encapsulated foci, the cure can only be considered as relative. Now, it has been shown, by means of inoculation tests, that if these foci contain caseous material virulent bacilli are always present. Only absolutely fibroid scars, as well as thoroughly calcified nodules, proved to be sterile (Kurlow, Green). The consumptive may be said to sit upon a volcano. Until the capsules have become absolutely perfect and impervious barriers, every event which tends to weaken them, or to open up the defects in their architecture, may become the occasion of a further dissemination of the bacilli, of the lighting up of a fresh attack.

Nevertheless, it seems to me to be a little far-fetched to attribute a fresh outbreak of the disease, after a quiescence of years, to the resurrection of the bacilli imprisoned in the old focus, since we know that the life period of the bacilli is bounded by certain definite and narrow limits. In cultures their vitality varies with the nature of the media and with the activity of their growth, previous to inoculation; upon glycerin-agar they live about six weeks, and upon blood-serum, in spite of the best possible temperature, about half a year. Koch believed that they were rapidly destroyed within the organism, and Kitasato proved this to be the case in cavities. It seems, therefore, that recurrences of phthisis after a lapse of years are to be attributed to fresh infections (reinfections) to which the consumptive has exposed himself by a return to the old conditions of life. The danger of infection is increased by the fact that the ciliated epithelium, which originally afforded considerable protection, is largely destroyed in the first attack.

One of the ways in which we might bring about a cure of the tuberculous process would be to imitate the natural method above described, and endeavor to restrict the absorption of proteins, and confine them to the neighborhood of the tubercles. Clinically, we often find that the exudation of fluid into the pleura or the formation of a pneumothorax is associated with a temporary improvement, which can only be ascribed to a compression of the tuberculous area. The future must show whether the artificial production of similar conditions, perhaps by the immobilization of the diseased area of lung, would not exert a similar favorable influence (see "Therapy").

DEATH.

Death from consumption often comes quietly and painlessly. *Non moriuntur, uti ellychnium deficiente oleo extinguuntur.* The strength of the patient sinks slowly, and a few days before death there occur collapse-temperatures, which alternate with the pyrexial periods. The sputum sticks; the invalid wastes his strength in unavailing cough, being too weak to expectorate. Edema occurs, and the deficient respiration gives rise to cyanosis and symptoms of carbonic-acid poisoning. The sensorium may remain unclouded; the patient is aware of his approaching fate, but still tries to ignore it. In other cases there is a low delirium, or the patient may become maniacal, and finally he drops off into his eternal sleep.

Complications may bring it about that death is very much more painful. Severe chills, pains in the chest, difficulty in respiration, the choking of the patient by his own secretions, may all darken the last few days of life. Thrush or ulceration of the pharynx may make it painful or impossible to swallow; delirium sets in, and the last days may be occupied by an awful battle for existence, until in the end death wins the victory.

The cause of death is generally cardiac weakness, due to the general inanition, the fever, and the action of the toxins. In other cases it results from limitation of the respiratory area, with deficient oxidation of the blood, and carbonic-acid poisoning. Rarely, death follows upon profuse hemorrhages, with the symptoms of suffocation or of acute anemia. In rare cases perforation of the intestines, peritonitis, meningitis, etc., or thrombosis and embolism of the pulmonary arteries (Barety), entrance of gas into the vessels of a cavity, or uremia, may be the direct cause of death.

In marked contrast to the usual mode of death in consumption, which follows upon a prolonged struggle marked by progressive loss of strength and hectic fever, the end may come quite suddenly and unexpectedly, after a few days of brief but rapid decline. At autopsy one finds neither sufficient cardiac degeneration nor extensive enough pulmonary lesions to account for it.

Quite often, the body shows no real miliary tubercles, but, upon careful examination, numbers of minute microscopic nodules. Thus Brissaud and Toupet found them almost without exception in thirty livers from consumptives, and Arnold in every one of fifty autopsies. They are invisible macroscopically, and are evidently of recent formation, perhaps eight to ten days old. They point to an hematogenous dissemination shortly before death; possibly they are in part due to dead bacilli, which are known to produce such changes. Moreover, we know that dead bacilli are capable of producing death through marasmus within a very short time in healthy animals, while minimal quantities suffice to kill animals which are already tuberculous (Maffucci). I regard it as not at all improbable that death coming on rapidly and in the midst of health may be due to the rupture of some old tuberculous focus, and the absorption of its dead bacilli and their proteins into the circulation; in other words, to an acute intoxication (see page 301).

CHAPTER IV.

DIAGNOSIS.

In hardly any other disease is early diagnosis of such importance as in pulmonary phthisis. Time is everything. In the later stages, the disease betrays itself even to the untutored by the cough, expectoration, and emaciation. The early symptoms, however, are often very ambiguous and misleading. Physicians were, therefore, very apt to fall into error, and to reach a correct diagnosis only after their best chance had passed by.

ANAMNESIS.

A great deal is to be gained from a careful anamnesis, which should embrace not only the family, but the more remote environment. We have already expressed ourselves upon the subject of hereditary influences. With the possible exception of the rare events mentioned on page 325, we cannot recognize a specific hereditary predisposition. Children of tuberculous parents (*i. e.*, of parents who at the time of conception are already more or less tuberculous) will, of course, enter the world handicapped. This handicap, however, differs in nowise from that which besets children born of parents with any other form of disease, or from that which is acquired *intra vitam* through any untoward influence, and probably predisposes the individual to other forms of disease as well.

An anamnesis is worthless if it only establishes the existence of tuberculosis in the family, or even in the parents, unless it also determines the exact time of illness and of death. Even these data are useless, unless they bring out the details regarding exposure to which we have previously drawn attention. We must know exactly to what extent and for how long a period the invalid associated with the previous consumptive during the course of the disease. We should know whether the sputum was properly disposed of, how far back the association dates, etc. If we take up the anamnesis in this manner, if we extend it not only to the family, but beyond, to the school, factory, workplace, dwelling, we shall perhaps increase our labor, but we shall also obtain important results.

The fact that the anamnesis gives no positive results does not in anywise speak against tuberculosis. An exaggerated estimate of the influence of heredity and of inherited weakness has worked to the detriment of many a consumptive. If the patient comes from a healthy family and looks strong, many physicians are afraid to diagnose tuberculosis. They prefer to speak of a catarrh or a bronchitis. If the bronchitis remains obstinate, or the patient steadily grows worse, or a hemoptysis occurs, the tuberculosis can, of course, no longer be questioned. If, however, the physician had made an examination of the chest and the sputum, instead of working upon a preconceived idea, he might have made an early diagnosis and also spared himself the reproach of carelessness. Only recently I met with two such cases.

PHYSICAL EXAMINATION.

In spite of a negative anamnesis, we should invariably examine the chest of a patient as soon as his complaints suggest intrathoracic disease.

The information which we may expect to gain from inspection and palpation has already been described in a special chapter (see page 416). Percussion and auscultation have also been treated in detail. It may be well to recapitulate that the earliest signs of a commencing tuberculosis, viz., dulness, diminished respiratory murmur, bronchial respiration, and râles, are almost always found at the apices; these should, therefore, always be examined with the greatest care, and every variation from the normal regarded as suspicious of tuberculosis. One must not forget, however, that the earliest foci occasionally appear in other parts of the lung,—*i. e.*, the middle lobes,—and the examination should, therefore, always embrace the entire lung.

EXAMINATION OF SPUTUM.

DEMONSTRATION OF TUBERCLE BACILLI.

The sovereign resource in making an early and correct diagnosis of tuberculosis is the demonstration of the bacilli in the sputum. The inspiration of tuberculous dust results in a tuberculosis, only if the bacilli are not immediately driven out again, but are permitted to settle and gain a foothold. The first of these two events occurs in the upper air-passages and the larger bronchi, while the second results when they succeed in reaching the alveoli, which have no ciliated epithelium and are, as it were, dead spaces. We might, therefore, expect to find such expelled bacteria in the mucus of healthy people. Practically, this possibility may be neglected. The examination might perhaps give positive results in a sound individual, in case he had just come from an atmosphere highly laden with bacilli, as in the cases cited by Straus or in the inhalation experiments of the author (see page 151). Bearing this possibility in mind, one may count the presence of tubercle bacilli in the sputum a sure sign of the disease, while their absence does not exclude it.

In examining the sputum, one saves himself much trouble by not accepting every specimen offered, perhaps the nasal secretion, but taking only sputum which comes from the deeper passages and to which no water has been added. In mucoid sputum one should pick out the thick, yellowish spots or streaks, or the tiny clumps, which often consist of pure cheesy material. The best plan is to spread out the sputum in a glass dish (Petri dish), over black paper, or in a black porcelain dish.

There are a number of methods of demonstrating the bacilli: The methods of Ehrlich and of Ziehl-Neelsen, both excellent,—the latter, however, simpler and better adapted to practical requirements,—have been already described (see page 28).

A further simplification consists in the combination of decolorization and counter-staining, as illustrated in Gabbet's method. A selected particle of sputum is rubbed upon a cover-slip, dried, fixed in the flame; it is covered with a concentrated Ziehl's solution (1 gm. fuchsin, 10 gm. absolute alcohol, 100 cc. 5 per cent. watery carbolic acid), and warmed until a heavy vapor rises; the stain is then washed off in water, and treated for five to ten seconds in the second solution (25 cc. sulphuric acid, 100 cc. water, and 1 to 2 gm. methylene-blue), again washed, dried, and examined. There is some ground for the objection of Heim, P. Guttmann, and Czaplewski, that the preparations are not so pretty as when the processes are kept distinct, and that some bacilli are lost by being over-decolorized. Nevertheless, the method is safe enough for most cases, and I would recommend it to the practising physician, except for permanent preparations; it is very rapid (hardly two minutes), and, if positive, suffices for diagnosis.

Often these methods reveal bacilli at the first trials. If, however, the results are negative, or the sputum consists almost entirely of mucus, it becomes necessary to render it homogeneous and then practise sedimentation.

According to Biedert, 15 cc. of sputum, 30 cc. of distilled water, and 4 to 8 drops of caustic potash or soda, are thoroughly stirred up together with a glass rod, kept at a low heat in an evaporating dish with the gradual addition of 60 to 90 cc. of distilled water, and finally allowed to settle for twenty-four to forty-eight hours in a conical glass. The sediment often fails to adhere, in which case one may fix it to the cover-slip by means of albumen or the sputum of the patient.

Other methods have been suggested by Mühlhäuser, Stroschein, van Ketel, Dahmen, and others. Van Ketel mixes 10 cc. of water, 6 cc. of liquefied carbolic acid, and 10 to 15 cc. of sputum, shakes the mixture well for one minute, and lets it settle for twelve to twenty-four hours. Heim renders it homogeneous, and sterilizes it at the same time, by exposing it for five to ten minutes to steam in enameled metal bowls in the receptacle suggested by Kirchner.

It is wise, especially where there are few bacilli, to hasten and complete the process of sedimentation by means of the centrifuge of Stenbeck-Litten, which is of great assistance.

The number of bacilli in the sputum varies extremely. The method of Ritter is of great assistance in getting at a general idea of the number of bacilli present, and in comparing the results of a series of examinations. His formula is a fraction, of which the numerator expresses the number of bacilli found, and the denominator the number of fields: *e. g.*, $\frac{1}{4}$ means 1 bacillus in 4 fields of vision, or $\frac{20}{1}$ means 20 bacilli in each field.

This method is more exact than the scale suggested by Gaffky, according to which 1 means one to four bacilli in the entire preparation; 2, only one bacillus in several fields; 3, about one bacillus in every field; 4, two or three; 5, four to six; 6, seven to twelve; 7, fairly many; 8, many; 9, very many; and 10, enormous numbers of bacilli in every field.

[As an aid to the early diagnosis, in cases in which tubercle bacilli cannot be found in the sputum, Hesse* recommends the following procedure, called enriching, and intended to cause the bacilli, if present, to multiply. Make up a nutritive medium as follows:

Heyden's Nährstoff	5	gm.
Salt	5	"
Glycerin	30	"
Agar-agar	10	"
Normal soda solution	5	cc.
Distilled water	1000	"

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* Zeit. f. Hygiene, July 31, 1899.

Then put about 20 cc. of this material into a double Petri dish. Have the patient expectorate into a sterilized glass; take up a mass of sputum, the size of a bean, by means of a platinum wire, and draw it about in a circle on the surface of the above culture-medium. Leave in an incubator for forty-eight hours; after that, examine the mucus in the usual way for tubercle bacilli.

Moeller* recommends the following method of enriching: He spreads several flecks of sputum on the bottom of a Petri dish, which is then put into a moist chamber to prevent drying, and the whole placed in an incubator for forty-eight hours. The tubercle bacilli are most easily found on the under surface of the flecks of sputum.

Wanner† has recently made elaborate chemical analyses of the sputum in phthisis, and arrives at some interesting conclusions.

First, that the albumin of the sputum in phthisis is derived from the tubercular lesion, and is in general proportionate in amount to the extent of this; and that the presence of any considerable amount of albumin helps establish the diagnosis of phthisis as against chronic bronchitis.

Second, that the proportion of mucin in the sputum in phthisis is less than in chronic bronchitis and pneumonia.—Ed.]

ANIMAL EXPERIMENTATION.

In those cases in which the microscopic examination does not help us, but in which there are good grounds for suspecting tuberculosis, animal experimentation offers an almost perfect, though much more laborious, diagnostic criterion.

The mode of procedure is as follows: If one wishes to establish the tuberculous nature of a fluid or of substances in emulsion, one should always resort to intraperitoneal injection. This method is the most favorable for the development of small numbers of bacilli, excludes infection most thoroughly, and presents an anatomical picture which is most easy to differentiate from a spontaneous infection of the animal. The guinea-pig is in every way the most suitable animal for these tests.

One side of the animal's belly, over an area about as large as a dollar, is shaved, thoroughly washed and disinfected with soap, alcohol, and sublimate. The suspected material, secured under antiseptic precautions, and held in fine suspension in about 2 or 3 cc. of a sterile fluid, is injected by means of a sterilized (Koch's) syringe into the body-cavity, and the site of puncture covered with collodion. If one suspects numerous living tubercle bacilli, the animal is killed after three or four weeks; if few, after about seven weeks. The autopsy determines the character of the fluid. For the anatomical picture, see page 103. (With experience, one learns to feel the enlarged spleen and omentum *intra vitam.*)

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* Münch. med. Woch., Dec. 10, 1901.

† Deut. Arch. f. klin. Med., Bd. 75, 1903.

If the material does not lend itself to suspension, one may resort to subcutaneous inoculation. The abdomen is prepared in the same fashion as before, a small incision is made in a fold of skin with scissors, and then a powerful platinum loop, which has been sterilized and cooled, is shoved to and fro under the fascia, between skin and muscle, so as to form a pocket about 2 cm. long. Into this the material is inserted, having been previously comminuted, and the external wound is sewed and covered with collodion. In many cases a swelling of the corresponding inguinal glands can be made out within eight to fourteen days. The animal is killed in five to nine weeks. For the anatomical picture, see page 99.

Intraocular injections are less to be recommended, not only because they demand greater experience on the part of the operator, but because unavoidable contaminations, *e. g.*, in mixed infections, may easily produce a phthisis bulbi, and so vitiate the entire result.

Animal experiment is so simple as to invite its use, and so certain that one wonders it is not more frequently invoked in doubtful cases. Keeping guinea-pigs is not a difficult matter. They may be kept in a cage, or, if this is not at hand, in a wooden box, and fed on carrots, and bread soaked in milk, and liberally supplied with hay and straw.

Formerly one had to be satisfied with finding elastic fibers. They occur most frequently, but by no means exclusively, in pulmonary phthisis; their presence is of value as indicating the degree of destruction. In looking for them, the sputum is mixed with an equal quantity of liquor potassii or a caustic soda, heated in an evaporating dish, allowed to settle or centrifugalized, and the precipitate examined under a magnification of 50 to 100 diameters, with closed diaphragm.

Coppen Jones found that tuberculous sputum often contained, in addition to the elastic fibers, a mycelium, the nature of which was not determined.

The presence of tubercle bacilli in the sputum presupposes that tubercles have broken down, and that their products have found a way to the exterior. If this fails to occur, or occurs in very limited measure, the sputum contains no bacilli, or so few that they are apt to escape detection. There may, notwithstanding, be an active process, which advances along the lymph-channels. Miliary tuberculosis of the lungs, also, rarely gives rise to bacilli in the sputum. The organisms may appear to be absent in cases in which the sputum is swallowed, *e. g.*, in children and many women; they may then, though with difficulty, be found in the feces.

In cases in which there is a suspicion of tuberculosis, and in which not enough sputum is expectorated, one should never neglect to investigate the feces.

TUBERCULIN AS A DIAGNOSTIC TEST.

Injections of tuberculin often clear up the diagnosis in cases which baffle every other means at our command. I prefer to use the original tuberculin of Koch. It is a striking fact that diagnostic inoculations are much more frequently employed by veterinarians than by physicians. The numerous researches upon this subject can be only briefly summarized; they show that tuberculous individuals react to the injections with fever, and with swelling and exudation locally, but that some cases fail to react in spite of the presence of the disease. These latter exceptions, however, are rare, and are chiefly contributed by individuals with healed encapsulated foci, or with such far-advanced processes that the test is superfluous. On the other hand, those cases in which the reaction was positive, but in which the disease failed to develop, leave it an open question whether a latent focus was not actually present. The tuberculin reaction does not, indeed, inform us of the location of the focus, whether in the lung, the bronchial glands, or elsewhere, but this difficulty may occasionally be cleared up by auscultation during the period of reaction.

The temperature of the patient is taken every two hours for three days before the injection, in order to get an idea of its variations. One milligram of tuberculin is then injected at night. The reaction is to be expected within eight to sixteen hours. On the next day the temperatures are again taken every two hours. If there is no reaction, it is well to wait one to two days, since the reaction is occasionally retarded. On the fourth day 3 milligrams are injected; and, if the results are negative, on the seventh or eighth day, 6 milligrams. If there is still no reaction, tuberculosis is in all probability absent.

[In the past three years tuberculin has been very extensively used for diagnosis, and the experience of many observers has been published. It is generally admitted that Koch's old tuberculin is still the best preparation for the purpose. The solution keeps well undiluted. Before being used it should be diluted with a sufficient quantity of 0.5 per cent. carbolic acid solution, but it must be remembered that such a dilution is absolutely trustworthy only for two or three days after being made up. In adults tuberculosis cannot be positively excluded unless up to seven milligrams have been given without producing the characteristic reaction. More than ten milligrams should never be given.

It should be remembered that after several doses of tuberculin an individual becomes partially immunized to its action, so that the reaction may not appear, although tuberculosis be present. This fact has been made use of by unscrupulous cattle dealers, who immunize tuberculous animals to tuberculin by repeated injections before the test immediately preceding sale is applied. It is best to give the injection late at night, since the reaction sets in about twelve hours later.

The value of this agent in the diagnosis of obscure cases has become more and more firmly established, and its harmlessness, when properly used, has been proved by the results in many thousands of cases. It should never be given in cases with fever, or in cases in which a previously active tuberculosis has only recently become latent.

Moeller and Kayserling* use tuberculin freely, both for diagnosis and for treatment, and regard it as a valuable and harmless agent. They call attention to the fact that recent cases, even if slight, react to a very small dose, and give a good reaction; while chronic cases of long standing, even if there be considerable disease, require larger doses, and give a relatively slighter reaction. Tinker† reports the results of the use of tuberculin for diagnosis in four hundred surgical cases. He found the test was never harmful except in very large doses. It was of great value in differentiating tuberculous disease, especially from hysterical, rheumatic, and traumatic lesions of the joints. No one of nine cases of Hodgkin's disease in which it was applied reacted. No reaction was obtained in actinomycosis. In this series of cases they met with no evil effects. The doses used were 2, 3, and 5 milligrams.

It is the experience of the editor that changes in the physical signs, the appearance of new signs, or an increase of those previously

* Ztschft. f. Tuberc. u. Heilst. vol. iii, 1902, p. 279.

† Johns Hopkins Hosp. Rep., vol. xi, 1903.

present occur much less often in association with a positive reaction than is usually supposed to be the case, and, indeed, are not usually to be expected.—Ed.]

FEVER.

One of the most important points in diagnosis, and, as I may add, in therapy, is the early and exact estimation of the temperature. The great importance of this symptom warrants the utmost care in determining it. The pulse, of course, constitutes a very unreliable index of that temperature. Measurements taken under the tongue with the mouth closed, especially if there are variations of only a few tenths of a degree, are not so reliable as measurements in the axilla. Rectal temperatures are, of course, more reliable than any others; unfortunately, they cannot be obtained in ambulatory cases.

The temperature, as is well known, varies with the time of day, being lowest in the morning and rising toward afternoon. The normal maximum varies, also, with the individual, and depends to a certain extent upon age. In some individuals it barely attains 37° C. (98.6° F.), and 37.3° C. (99.1° F.) denotes a febricula; in others, the norm goes as high as 37.5° (99.5° F.). It would be very much easier to appreciate the variations, if the temperatures had been followed during the previous era of good health. I should, therefore, strongly urge physicians to acquaint themselves with the diurnal variations of their patients during health. Unfortunately, the previous temperature is in most cases unknown, so that we must content ourselves with the average maximum of 37° C. (98.6° F.) to 37.3° C. (99.1° F.). Temperatures over 37.5° C. (99.5° F.) must, however, be regarded as a febricula, and be treated accordingly.

HOW OFTEN TO TAKE TEMPERATURE.

It is very generally the rule in private practice, in institutions and in clinics, to measure the temperature three times a day. After fourteen years of observation directed to this point, I venture to state that in a large number of cases this does not register the temperature with sufficient accuracy. I fully agree with Brehmer, who held that temperatures should be taken every two hours.

It is illogical to emphasize the importance of the fever in tuberculosis, to assert that it may come at any time, may amount to only a fraction of a degree, and may last only a few hours, and then to content one's self with three measurements a day—morning, noon, and night.

During the course of the year I have observed a large number of consumptives who had 36.6° C. (97.8° F.) at 8 A. M., 37° C. (98.6° F.) at 12, and 36.9° C. (98.4° F.) at 6 P. M.; in other words, an apparently normal temperature, whereas a two-hourly measurement showed a rise to 37.7° (99.8° F.) and over at about 3 P. M. This small rise may betray itself by a feeling of discomfort, or may run along for weeks unnoticed; eventually, as the fever becomes higher and more continuous, it affects the evening and morning measurements. It seems, therefore, far more reasonable to take more frequent measurements, in order to detect the rise before it becomes pronounced and before the damage has been already done. In fever, above all things, the axiom holds: *Principiis obsta.*

I cannot urge too strongly, therefore, that the measurements should be made at least every two hours, for the sake of those consumptives—of whom there are not a few—in whom the rise does not happen to coincide with the tri-daily measurements.

Inasmuch as the physician cannot take the measurements in person every three hours, the patient must learn to do so himself. It is rare to meet a patient who cannot master the art. It is even better to entrust the duty to one of the family or to a nurse, so that the patient may not be made aware of his condition. We must not sacrifice all our intelligent patients for the sake of those few misled individuals who develop an actual mania for the thermometer, and we certainly do sacrifice them, unless we recognize the pyrexia in time.

I should not advise the two-hourly measurements in a case in which the patient becomes very anxious, or the temperatures cannot be taken by another person, or the disease has already gone so far that effort seems vain and the measurements an unnecessary annoyance.

If the temperature remains normal for about five days in succession, I then take it only every second or fourth day in patients who are out of bed, or after a time even at longer intervals, but always every two hours throughout the day, preferring this method to three measurements every day.

Inasmuch as it is our primary object to determine whether the temperature oversteps the normal, and is only of secondary interest to know when the rise occurs and how long it lasts, I have devised a maximal thermometer, which is placed in the axilla and registers the daily maximum. In this way we avoid disturbing the night's rest of the patient.

Temperatures of 37.7° C. (99.8° F.) to 37.9° C. (100.2° F.), which are intermittent but obstinate, and which increase upon the slightest exertion, indicate tuberculosis, unless some other etiological factor can be discovered. I am able to confirm in all essentials the conclusions reached by Höchstätter under Penzoldt's guidance. He found that moderate exertion sufficed to produce a rise of temperature in consumptives otherwise free from fever. In a trip to a place three kilometers away and 100 meters higher than the starting-point, the double journey being made in an hour and a quarter, consumptives showed a difference between the temperatures taken at the start and the return almost twice as great as that found in the healthy individuals who served as controls. It seems not improbable that this fact may become of diagnostic value.

The fever of tuberculosis is characterized by a pulse which is extraordinarily rapid, and irregular, especially in response to psychical or physical excitation (increased absorption), and is distinguished by this fact from the other infectious diseases, *e. g.*, typhoid. This is explained in our definition of tuberculous fever (see pages 383 and 388). High fever without mental symptoms, if tuberculous in origin, is generally cleared up by the physical examination.

The typus inversus, according to Brunniche, is especially characteristic of acute miliary tuberculosis, but is occasionally found in malaria. Tuberculous fever resembles the latter to a certain extent in the chill and the profuse sweating, but is ordinarily not so high, is irregular, often intermits incompletely, is unaccompanied by a splenic tumor, and does not yield to quinin. Nevertheless caution is advisable in malarial districts (anamnesis). A short, dry cough, a febrile dyspnea, and a rapid general decline, point to tuberculosis (v. Sokolowski).

As a rule, the fever of tuberculosis has a period of a single day. Occasionally, however, I have seen consumptives whose fever had a cycle of two to four days, over a considerable period of time, so that the maximum on the first day would be 37° C. (98.6° E.); on the second, 37.8° C. (100° F.); on the third, 38.1° C. (100.6° F.); and on the fourth, 38.4° C. (101.1° F.); and the fever would then gradually decline in the same fashion. Severe sweats, especially toward morning or evening, are always suspicious.

Of great importance is the prolonged observation of the body-weight. If a man takes sufficient nourishment and yet constantly loses weight, one is justified in suspecting tuberculosis, unless there be some other evident cause, *e. g.*, diarrheas.

COUGH.

Dry or hacking cough, obstinate and repeated choking spells, or cough with vomiting, always demands thorough and repeated examination of the lungs, especially the apices. Purely nervous (non-tuberculous) cough is almost always accompanied by other nervous or hysterical symptoms. It is apt to be excessively severe, to change rapidly, to cease suddenly, especially if the mind be distracted, to disappear at night, and to be displaced by other nervous phenomena. In spite of its chronicity, it has a very slight effect upon the general condition and the weight, does not alter the physical findings, is often distinctly dependent upon the menses, and usually yields to hydrotherapy, iron, and change of air.

Excessive cough, with marked emaciation, may be due to tenia. Hérard, Cornil and Hanot describe such cases, in which there were stormy attacks of cough, which refused to yield until the tenia had been removed. Dyspnea at times produces a stomach-cough, which is accompanied by paroxysms, especially in the evening, and even by pronounced emaciation (Trousseau). This may arouse a suspicion of phthisis, which the physical examination alone can decide.

Even though it seems possible, at the time, to exclude tuberculosis with certainty, one should not remain satisfied, but should repeat the examination at not too distant intervals, since the primary heterogenetic cough may eventually become combined with a tuberculous cough.

HEMOPTYSIS.

In the vast majority of cases hemoptysis speaks for pulmonary tuberculosis, although it is not absolutely pathognomonic. It may also result from circulatory disturbances and stasis in the pulmonary circulation due to cardiac lesions. At times it replaces hemorrhoidal or menstrual bleeding, or accompanies the latter. Hysterical individuals not rarely have bloody sputum periodically, or for weeks at a time, with no disease in the lungs. Hemoptysis without tuberculosis may also occur after severe exertion,—a long march, exercising, mountain-climbing, or dancing,—excesses in *Venere et Baccho*, abuse of tea or coffee, or after a trauma.

Hemorrhages from the mouth, throat, gums, or nasopharynx may be diagnosed by their admixture with saliva, by the superficial location of the clots, and by a thorough inspection of the cavities (hyperemia, varices). Ordinarily such hemorrhages are very slight.

Larger hemorrhages can be confused only with bleedings from the stomach. Blood which comes from the stomach is mostly darker in color, although blood which has been in the lung for a considerable time also becomes dark; it is mixed with food, and is vomited out (see page 371).

Various as are the possible causes, in practice one will rarely err, if a patient feels a sudden tickling in the throat and then coughs up foamy blood mixed with air, in assuming that a pulmonary tuberculosis is present, and treating accordingly.

DYSPNEA.

Dyspnea develops only when the disease is well advanced, or in connection with an acutely progressive miliary tuberculosis of the lungs. Otherwise, in the absence of marked physical signs, one must think of pressure upon the vagus or the bronchi by swollen caseous glands, by tumors, etc., or of nervous influences, or of chlorosis. Pleurisy, pneumothorax, and emphysema may be easily identified by their physical signs. Paroxysmal dyspnea points especially to asthma, stenocardia, and similar conditions.

HOARSENESS.

Of diagnostic importance is obstinate although often slight hoarseness, which sometimes precedes all the pulmonary symptoms. The laryngoscope reveals a unilateral or double paralysis of the vocal cords; the cords are of the normal white color, not reddened or swollen. The paralysis is due to the pressure of tuberculous lymph-glands upon the vagus.

The unilateral paralysis, which is an occasional sign of beginning pulmonary tuberculosis, is to be distinguished from the paralyses which depend upon a luetic or catarrhal basis. In the luetic variety there are other signs, such as the mucous patches or the characteristic coppery redness of the laryngeal mucosa, or the anamnesis may suggest lues. In the catarrhal pareses the cords are reddened, while they are generally of a normal white and the mucous membrane anemic in the initial stage of phthisis.

With such phthisical paralyses there are also, according to Schäffer, an indefinite feeling of pressure and a sort of rheumatic pain over the thorax. Slight associated catarrhs disappear, while the paresis persists, involving chiefly the narrowers of the glottis. The patients are ordinarily hoarse only toward evening; at first they hawk a good deal, and later develop an irritative cough.

Hysteria also, as is well known, leads to paralyses of the vocal cords, but the hoarseness is manifest in speaking rather than in coughing. There will not often be room for confusion with the paralyses due to central lesions, or with those due to neuritis of the recurrens, as in diphtheria or the other infectious diseases, or in lead-poisoning, or with those due to pressure, as by an adenitis or a periadenitis, or an intrathoracic tumor (especially the left nerve), *e. g.*, a gumma, a carcinoma of the esophagus, an aneurysm of the aorta.

Since the lung offers the passage by which the tuberculous virus finds its way to the glands, it is easy to understand that phthisis upon the same side is apt to follow a paresis due to pressure of the glands.

DIMINUTION IN VITAL CAPACITY.

The attempt has often been made to employ the spirometer in the diagnosis of phthisis. Since, however, there are a number of factors which produce variations of the vital capacity even under normal conditions, it follows that any deductions are to be made only with the utmost caution.

In doubtful cases spirometry is of great assistance if it discloses a marked variation from the normal values, and a diminution of the proportion between pulmonary capacity and height to less than 1:18 in men and 1:15 in women. It is assumed, of course, that the other diseases which likewise compromise the vital capacity have been excluded: such are pleurisy, emphysema, pulmonary cirrhosis, bronchitis, and all those affections of the lungs, pleura, heart, and intestines which serve to cut down the free space within the thorax. On the contrary, an increase of the ratio over 1: 22 in men and 1: 19 in women would argue to a certain extent against tuberculosis (see page 437).

Of greater importance is the part played by spirometry in informing us of the progress in any individual case, although one must always keep in mind the fact that the vital capacity of the patient may increase through exercise.

In determining the vital capacity, I proceed as follows: The patient removes all tight clothing. For a mouthpiece I prefer a smoothly polished tube of horn to the usual mouth-mask. The patient stands upright, and, after a few trial breaths, takes in as much air as he can hold, and then, with the mouthpiece held closely in the lips, forces it slowly, and with as much power as he can command, out into the spirometer. This attempt is repeated a number of times, until the result remains fairly constant.

I am unable to confirm the objection of certain authors, that spirometry requires so much skill and experience as to be excluded in the vast majority of cases. I do not agree with Wintrich in taking the average of the tests as a measure of the vital capacity, but rather the maximum figure, since this indicates the amount of air-space in the lungs at the moment of most perfect inflation.

[SERUM REACTION.

Arloing and Courmont* in 1898 called attention to the fact that the blood of rabbits and goats that had been treated with tuberculin caused agglutination of tubercle bacilli that were suspended in a bouillon culture. They also claimed that the same phenomenon was produced by the blood of many cases of pulmonary tuberculosis. At the Berlin Congress for Tuberculosis, Courmont recommended the employment of this method in diagnosis, and advised the use of serum in dilution of 1:10 or 1:20. Later the above two authors reiterated their claim that, while not invariably negative, nevertheless the reaction generally occurred, and was of use in diagnosis.

Since this time a great many observations have been published (Fränkel,† Beck and Rabinowitsch,‡ Koch,§ Wright,|| Hawthorne,** de Grazia,†† Romburg ‡‡ and others). While a few observations have supported the conclusions of Arloing and Courmont, the majority have failed to do so, and the method must be regarded as of no practical value as an aid to diagnosis—first, because a large number of cases of tuberculosis even in advanced stages fail to give the reaction; and, second, because many non-tuberculous cases do give the reaction. Koch especially has made elaborate experiments, both upon human beings and upon cattle, and concludes that it has no value in diagnosis.

Henkel§§ recommends that in doubtful cases, from which no

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* Congres pour l'étude de la Tuberculose, 1898; Deut. med. Woch., 1900, p. 766.

† Hyg. Rundschau, 1900, No. 13.

‡ Deut. med. Woch., 1900, p. 400; ibid., 1901, p. 145.

§ Deut. med. Woch., 1901.

|| Lancet, May 9, 1903.

** Compt. Rend. Soc. de Biol., 1903.

†† Berl. klin. Woch., 1902, Nos. 11, 12.

‡‡ Münch. med. Woch., 1902, No. 3.

§§ Münch. med. Woch., 1900, No. 13.

sputum can be obtained, the apex of the suspected lung be aspirated by an exploring needle and syringe. He believes that this procedure is justified, and is accompanied by no danger. No bleeding has at any time followed the procedure, but sometimes there is a temporary rise of temperature. It is not a method that will appeal to most reasonable physicians, nor one to which the public would generally be willing to submit. The chances of obtaining a material that would enable the diagnosis to be made are slight, while the method could hardly be regarded as free from danger. As a diagnostic procedure it is not to be compared in efficacy or harmlessness with the injection of tuberculin.

In obscure cases without characteristic physical signs, and in which the sputum is scanty and does not contain tubercle bacilli, Vetlesen* recommends the use of iodid of potash for the purpose of increasing the amount of sputum and developing râles in an apical lesion where they did not previously exist. He reports twenty-seven cases of this type, in eight of which a positive result was obtained after the administration of the iodid of potash. He claims that it produces a catarrh, resulting in the appearance of râles at the apex of the lung, and the appearance of bacilli in the sputum. Wells† has found that this procedure produces the results claimed by Vetlesen.—Ed.]

MASKED FORMS.

The diagnosis of pulmonary tuberculosis is most difficult in those larval forms which present a symptom-complex having apparently not the slightest connection with disease of the lungs.

CHLOROSIS.

Very frequently, especially in young girls, pulmonary tuberculosis in the earlier stages gives the picture of chlorosis. Lack of energy, a feeling of tiredness, increase in the rapidity of the pulse and of respiration, and nervous dyspepsia, are prominent features of both conditions, and may make it very difficult to differentiate between true chlorosis and a tuberculous pseudo-chlorosis (*chloranœmie tuberculeuse* of the French). Even emaciation may occur in chlorosis, although an increase in the fatty tissue is more frequent. It is doubtful whether we can lay much stress on the color, which in chlorosis is rather greenish (Sée), and in tuberculosis is a dirty yellow.

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* Rev. Cent. f. innere Med., 1898, p. 999.

† Jour. Am. Med. Assoc., Feb. 4, 1899.

Temperature, also, affords no positive differential criterion. Chlorosis, it is true, generally runs an afebrile course, but a series of cases has been described by Wunderlich, Eichhorst, von Noorden (in about 80), and others, in which there were rises of temperature up to 38° C. (100.4° F.) and 38.5° C. (101.3° F.); on the other hand, the early stages of pulmonary tuberculosis are often afebrile. The frequency of venous murmurs, especially over the jugular vein, in chlorotics, is not of differential importance. Dysmenorrhea is in general more characteristic of chlorosis than of tuberculosis; in the latter, the menses tend to become less profuse, and finally to be omitted. Even the examination of the blood may at times yield the same result in the early stage of tuberculosis as in chlorosis.

At times a careful anamnesis is of great assistance, inasmuch as it establishes the possibility of an infection. A history of scrofulous glands, or of an ineffective iron-cure, speaks for tuberculosis. The most important differential point, however, as von Noorden has recently brought out, is the result of the injection of tuberculin; if there be no reaction, tuberculosis may be excluded with an approach to certainty.

NERVOUS DYSPEPSIA.

There are difficulties in the diagnosis of that form of pulmonary tuberculosis which at first gives only the symptoms of a nervous dyspepsia, namely, loss of appetite, vomiting, epigastric pain, and flatulence, without any other functional or motor disturbance. In purely nervous dyspepsias the loss of appetite is generally less complete than in tuberculosis, and more capricious. Slight afternoon rises of temperature point to tuberculosis, as does marked emaciation; the weight remains fairly constant in the purely nervous dyspepsias, since the assimilative processes are not disturbed.

When diarrhea is an early symptom, it is sometimes possible to find tubercle bacilli in the feces (especially in children and the insane).

NEURASTHENIA.

An initial phthisis may mimic neurasthenia, and, vice versa, neurasthenia may imitate the exhaustion, night-sweats, anorexia, and "run-down" appearance of phthisis. If, in addition, there is a weak, tired voice, as a consequence of the loss of tone in the laryngeal muscles, and pain in the thoracic muscles, the neurasthenic himself entertains no doubt that he is suffering from an advanced form of consumption. "In the morning hectic, in the evening electric."

The differential diagnosis depends upon the anamnesis, the physical status, the contents of the sputum, and the reaction to tuberculin.

A striking example of this difficulty has been observed by me at intervals during the last ten years. The patient had apparently had an attack of tuberculosis some time before. Over the upper part of the right lung behind, there was a slight flattening of the apex, and a roughened, somewhat bronchial expiration. These conditions were somewhat luridly described to the patient by a physician who was not acquainted with the antecedents of the man, and from that time on he had a firm conviction that he was suffering from pulmonary tuberculosis. At intervals he put himself into an institution for pulmonary diseases, and received incredible quantities of creasote. Although only of middle height, he weighed over 200 pounds, yet nothing would move him from his conviction until I had given him tuberculin injections. As I expected, these produced no reaction, and were successful in curing the patient of his phthisiophobia.

PLEURISY.

Sometimes pulmonary tuberculosis first appears in the guise of a pleurisy. Even then, however, it betrays its character by the markedly remittent fever, the night-sweats, the loss of weight, and the friction-râles and pains often confined to the apex. If an exudate forms, it is generally small in amount, serous, clear, and apparently sterile. At times, it is only after the removal of the exudate that the real disease of the apex becomes evident, through catarrhal symptoms and sputum.

DIFFERENTIAL DIAGNOSIS BETWEEN PULMONARY TUBERCULOSIS AND OTHER DISEASES OF THE LUNGS AND BRONCHI.

The diagnosis becomes somewhat easier when the symptoms point to the lung as the seat of disease. In the first place, the examination of the sputum paves the way to a more definite diagnosis. The conditions from which it is most important to distinguish tuberculosis are acute and chronic bronchitis. In acute bronchitis the postero-inferior portions of the lung are generally involved, rarely the upper lobes or a single apex. Moreover, the symptoms persist below longest. The percussion note is unchanged. In contrast to tuberculosis, appetite and nutrition are not markedly disturbed. Proper treatment is followed by speedy recovery.

The same points, notably the physical signs, serve to differentiate a chronic bronchitis. Chronic tuberculosis almost invariably produces a chronic bronchitis, through the local irritation of the toxins.

In *bronchitis* with emphysema the inspiratory murmur is first roughened; in tuberculosis, the expiratory. In the former the sound over the emphysematous apex is often strikingly sonorous, the râles sibilant in character, and fever rare. The catarrh is very largely dependent upon the state of the weather and the humidity, and is subject to rapid variations.

Chronic pneumonia, especially such as is due to the influenza bacillus or to streptococci, may mimic a phthisis both in its entire course and in the constitutional disturbance to which it gives rise. The discovery of such micro-organisms is, therefore, of great importance; but yet does not exclude tuberculosis, inasmuch as the latter is often complicated by secondary infections of this kind. Ordinarily this pneumonia does not begin in the apices, but wanders there secondarily. Its migratory character is often characteristic. The discovery of tubercle bacilli, the result of tuberculin injections,—especially the local reaction,—and the inoculation of animals, furnish the critical diagnostic points.

There are still other groups of lung troubles which are associated with cough, expectoration, dyspnea, and pain, and occasionally with fever, progressive emaciation, and hemoptysis. If to these signs are added the physical evidences of infiltration or cavity-formation, the clinical picture of an advanced phthisis is very closely approximated. Since, however, there is question only of the late phases of phthisis, the doubt may easily be settled by an examination of the sputum for tubercle bacilli. Should the result be negative, or should there be a suspicion that there is some complication in addition to the tuberculosis, the following points are to be considered.

Bronchiectases are ordinarily distinguished from tuberculosis by the fact of their origin from a pneumonia or a pleurisy. They generally lie at the back and below, or in the middle lobe, rarely in the upper lobe; they are ordinarily confined to one side, phthisis in the later stages being bilateral; and they have a characteristic sputum. The balls of sputum do not remain isolated, but run together, and usually have an extremely fetid, sickening odor. Bronchiectases often leave the general health undisturbed for years, and are rarely accompanied by the general disorganization characteristic of tuberculosis.

Pulmonary gangrene is distinguished by the foul and disgusting odor of the breath and sputum, which pollutes the entire atmosphere.

A disagreeable breath such as is at times to be noticed in phthisis is not even to be distantly compared with it. The sputum is often voided in paroxysms, and contains numerous, sometimes large-sized, shreds of lung tissue.

In *abscess of the lung,* also, one takes note of the development of the disease, of the voiding of sputum by the mouthful, of the presence of large shreds of parenchyma, and of the numerous crystals of blood-pigment.

The differentiation from *pulmonary syphilis* is more difficult. The absence of bacilli must always suggest this possibility, while their presence does not exclude a combination of the two diseases. A careful anamnesis regarding preceding syphilitic and tuberculous infections, and a detailed examination of the body for other evidences of syphilitic scars, especially on the genitals, in the throat, on the skin, and bony irregularities, may often lead to the proper solution. Syphilitic infiltrations appear in the tertiary period, often only five to fifteen years after the primary infection (Fournier). They involve almost exclusively the middle lobes, or the middle part, of the lung, especially on the right side, according to Grandidier; they proceed from the glands of the hilum which explains the severe dyspnea, and the troublesome, often paroxysmal cough. Fever and loss of strength may be absent for a long time, and are often less marked than in tuberculosis. Destruction of a gumma leads to cavity-formation, which is distinguished by the absence of tubercle bacilli.

At times the diagnosis may be made by the success of an antisyphilitic cure. Langerhans relates such a case: a patient fell sick with the symptoms of a right-sided apical catarrh, and hemoptysis; the diagnosis of syphilis was later made *ex juvantibus.* In such cases the preference is to be given to potassium iodid, 2 to 5 gm. daily, which does not so seriously prejudice the course of a possible tuberculosis as does the use of mercury, and can cause the absorption of syphilitic foci inside of a few weeks. One may have to resort eventually to injections of tuberculin or to animal inoculation.

Cancer of the lung most often involves the right upper lobe, and starts from the hilum. Here, as in syphilis, the situation argues against an origin by inhalation, and speaks rather for the glands as the starting-point. Of diagnostic assistance are the presence or the history of carcinomatous deposits in other organs, the frequent involvement of the bronchial, supraclavicular, infraclavicular, and axillary glands, and the symptoms of their pressure upon the vessels (venous stasis, varicosities, especially to the right, anteriorly, and above), and upon the nerves (severe neuralgias, vocal paralyses), and upon the bronchi (urgent dyspnea). If the carcinoma be superficial, and of considerable size, the corresponding half of the thorax becomes enlarged. Expectoration is often small in amount, and reddish or dark-brown in color, like raspberry or currant jelly. The sputum in tuberculosis rarely has this character. At times there are carcinomatous fragments in the sputum. Softening gives rise to the signs of cavities. Moreover, cancer may occur in conjunction with tuberculosis, as Pirot and Sückling have described.

Echinococcus disease of the apex may also mimic a tuberculosis, both subjectively and objectively, with cough, expectoration, dyspnea, fever, emaciation, and signs of a cavity. A history of close association with the domestic animals may suggest echinococcus. The condition is often secondary to echinococcus of the liver, and usually involves the upper, rarely the lower lobe. The auscultatory changes are ordinarily slight, in spite of a considerable extension of the disease. The sputum is often fetid or bloody. The presence of parts of the sac or its content in the sputum is characteristic.

Actinomycosis of the lung may give rise to infiltration and to cavity-formation. Here, too, the process is usually confined to the lower lobes. The presence of the mycelium clears up the diagnosis. The absence of elastic fibers is noticeable. Eichhorst observed a case of pulmonary tuberculosis in addition to actinomycotic perityphlitis.

Anthrax of the lung is to be established by isolation of the bacillus and the inoculation of guinea-pigs.

[Janeway* reports an interesting series of cases, in which continued fever, with sometimes slight pulmonary symptoms, had led to the diagnosis of pulmonary tuberculosis, but in which the condition was the fever of late syphilis. He calls attention to the liability to this error, and advises in such cases, in which a definite pulmonary lesion cannot be made out, that an antecedent syphilitic history be carefully searched for, and anti-syphilitic treatment be administered.

Stengel† reports cases of syphilis of the lungs simulating pulmonary tuberculosis, and states that the differential diagnosis cannot be made with certainty, though in some cases the disease may be suspected. He says that it is important, however, to recognize that pulmonary disease presenting symptoms and physical signs practically identical with those of pulmonary tuberculosis may be due to syphilitic disease of the lungs; and that when the absence of tubercle bacilli in repeated examinations of the sputum and the presence of syphilitic lesions in other organs suggest the possible syphilitic nature of the disease, vigorous antisyphilitic treatment should be instituted with the hope of an occasional success.

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* Am. Jour. Med. Sci., 1898, vol. 116, p. 251.

† Univ. Pa. Med. Bulletin, May, 1903.

Berg* claims to have met with several undoubted cases of pulmonary syphilis, and believes that it is a much more frequent condition than is generally supposed. He finds that both the physical signs and symptoms closely resemble those of pulmonary tuberculosis, and believes that, in the absence of tubercle bacilli in the sputum, diagnosis can be made after the thorough administration of the iodid of potash.

Winfield† reports an interesting case of similar nature, in which the symptoms and signs closely resembled those of pulmonary tuberculosis, but in which the absence of tubercle bacilli in the sputum, and the entire disappearance of the trouble upon the administration of antisyphilitic treatment, appeared to justify the conclusion that it was a case of pulmonary syphilis.—Ed.]

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* Med. Record, Dec. 13, 1902.

† Med. News, Aug. 30, 1902.

CHAPTER V.

COMPLICATIONS.

BY DISSEMINATION OF THE BACILLI.

The course of a pulmonary tuberculosis is frequently marked by complications due to the extension of the infection. The lymphatics carry the bacilli to the bronchial glands, the pleura, and the pericardium; the sputum conveys them to the larynx, throat, nose, mouth, and especially the gut, or, occasionally, to the skin, the genitals, or the eye; the blood opens the way to all the organs.

GLANDS.

Tuberculosis of the bronchial glands may be regarded as a regular accompaniment, especially in infancy. If small, the diseased glands often produce no symptoms; but if they attain a sufficient size, they may give rise to symptoms referable to the compression of the nerves (vagus and recurrens), the vessels, and the bronchi. These are: tachycardia, a pertussis-like cough, rough or hoarse voice; in breathing, a feeling of pressure, of restraint, dyspnea, or orthopnea; in the circulation, venous stasis, especially of the neck and chest, a venous network on the anterior surface of the thorax (due to compression of the innominate), cyanosis, rarely edema of the face or of one or both extremities, epistaxes, and differences between the pupils.

Physical signs: diminution of the percussion-note between the second and fifth dorsal vertebræ; often very loud, indefinite, mostly bronchial breathing, even with the mouth closed, over the third and fourth vertebræ, which is occasionally found in very thin individuals in health, but not so distinctly.

More rarely, and especially in youth, the cervical glands are secondarily affected. Very often they are scrofulous before the lungs are diseased. They are easily accessible to inspection and palpation.

SEROUS MEMBRANES.

Tuberculous pleurisy may occur early, apparently in connection with the primary tubercle in the lung. It arises by extension from a superficial cheesy focus, or even by simple diffusion of the proteins.

If the irritation is less acute, there is a localized pleurisy, with adhesion of the opposite layers, which provides a certain amount of protection against further disturbance.

The clinical signs of a pleurisy are friction sounds, which are often confined to one apex. The formation of miliary tubercles in the pleura is evidenced, according to Jürgensen, by a peculiar, soft, and characteristic rub. For the rest, the symptoms are those of an ordinary dry or serous pleurisy. The exudate is often less extensive, serous or sero-sanguineous. When cavities are formed, other bacteria often find their way to the pleura (mixed infection) and modify the purely tuberculous pleurisy (empyema). If the fluid is rapidly absorbed, there are often fresh secondary invasions, such as an acute miliary tuberculosis (Litten) or tuberculosis of the bones and joints (Czerny).

Pneumothorax constitutes a fairly frequent complication of phthisis (5 per cent., Powell, West). It arises through the perforation of superficial caseous foci or cavities, with entrance of air into the pleura. A necessary preliminary is the rapid destruction of the caseous focus, as otherwise the irritation of the toxins causes a chronic inflammation and thickening of the pleura, and fibrous union of the two leaves. The perforation most frequently occurs between the mammillary and axillary lines, at the level of the fourth to the second intercostal space.

Often, but especially in slight processes, it takes place suddenly, after a forced expiration, a fit of coughing, or lifting a heavy load. The patient has a sticking pain, a feeling as though something had torn in his chest; he develops severe dyspnea, orthopnea, a fall of temperature with collapse, and lies on the diseased side, in order to give full play to the unhampered lung. All the physical signs may become suddenly changed. In other cases, especially in debilitated individuals, the pneumothorax develops very slowly, and it takes a most searching examination to discover it.

The process may either stop here, or may go on to the formation of a serous, hemorrhagic, or purulent exudate (sero-hemo-pyo-thorax). This difference simply depends on the nature of the material which finds its way into the pleura, whether sterile air from the lungs, or secretions containing bacilli or masses from old cavities rich in proteins, or mixed bacteria.

Physical examination shows an enlargement and immobilization of the affected side, displacement of the heart and liver, diminution of the vocal fremitus and bronchophony, and the other changes already mentioned in connection with auscultation and percussion (pages 420, 428).

In rare cases the pneumothorax has been followed by an improvement, but in general its influence upon the course of the disease is the more unfavorable, the further advanced the phthisis is. The end may come very rapidly, or may be brought about in a few weeks, with the development of an exudation, with decomposition.

The pericardium only rarely becomes involved. Cardiac pain, a sense of constriction, palpitation, pericardial friction sounds in case of a fibrinous exudation, enlargement of the area of dulness, and loss of the apex-beat in case of fluid, are the essential symptoms, just as in an ordinary pericarditis.

A peritonitis tuberculosa is, as it were, a tertiary symptom. The connecting-link may be a tuberculosis of the pleura, of the pericardium, of the diaphragm, of the genitals, or most often of the intestines and the mesenteric glands. It may be either circumscribed, *e. g.*, over an intestinal ulcer, or more diffuse.

The new symptoms due to the peritonitis are abdominal pain, often not very severe, vomiting, diarrhea and fever, and in children often pale stools containing fat (Berggrün and Katz), frequently friction rubs, and the well-known symptoms of a more or less encapsulated peritoneal exudate.

BRONCHI, TRACHEA, AND LARYNX.

The sputum often produces complications on its way to the exterior. The smaller bronchi, through which the sputum is forced, are the first in line of exposure. Bronchitis due to the irritation of the toxins, cheesy bronchitis, and peribronchitis are the results. The sputum, now enveloped in mucus, passes much more smoothly through the larger bronchi and the trachea. The latter become involved in the disease only toward the end, when the reflexes are lost, the ciliated epithelium out of action, and stagnation is marked. On the other hand, those parts are menaced which form angles or buttresses in the respiratory tract, or which are particularly exposed by their position; in the first rank of these is the larynx. The explanation of this fact has already been given (page 171).

While this book was being set up, a work of Krieg's appeared which demands especial mention. He observed 700 cases of tuberculosis of the larynx, of which 275 were unilateral; of the latter, 252, or 91.6 per cent., were on the same side as the affected lung. From this he argues that infection of the larynx by inhalation or sputum is excluded in the vast majority of cases, since this fails to explain the conditions. Krieg therefore assumes that the infection travels by way of the circulation, to wit, the lymphatics, from the lung, and that the direction of the current is in part retrograde.

Though this may hold true of exceptional cases, we cannot, for the reasons already cited, accept this explanation for the majority of them. We may imagine a swelling of the bronchial glands of the same side as the diseased lung, which affects the recurrens either by pressure or by the absorption of proteins; by this means arises a paresis or paralysis of the cords of the same side, which even a careful laryngoscopy may fail to detect, and, as a result, a less perfect elimination of the sputum from that half of the larynx.

Tuberculosis of the larnyx occurs in about one-third of the cases of phthisis. It is most frequent in the later stages, when the mucous membrane has been put into a condition of chronic inflammation by the constant coughing and the irritant properties of the sputum, and the ciliated epithelium has begun to feel the influence of the general debility.

The symptoms are tickling in the throat, rawness, severe cough, often throughout the twenty-four hours, sharp pains, which at times radiate to the ear, dysphagia, frequent choking, and local edema and dyspnea which may become fatal. The voice becomes hoarse and aphonic.

The laryngoscope reveals swelling, thickening, or ulcerations. The latter are very variable in size, and their walls are generally flat, of irregular outline, and often studded with papillary excrescences. They lie on the true cords (Gaul), the posterior wall, the interarytenoid space, the epiglottis, and the arytenoid cartilages. In addition to the tumefaction and ulceration, there are tuberculous vegetations, tumors, and miliary tubercles around the ulcers.

If phthisis is also present, the nature of the process can hardly be mistaken. The syphilitic ulcers of the larynx, which are most apt to be confused with the tuberculous, are distinguished by their sharp margins, their tendency to cicatricial contraction, and the frequent swelling of the cervical lymph-nodes. In lues the mucous membrane of the larynx and pharynx is often dark red, in tuberculosis anemic.

In doubtful cases tuberculosis may be diagnosed by an examination of the secretion, or, better, of particles of tissue taken from the ulcer, or by the detection of a local reaction (redness, swelling, exudation) upon the injection of tuberculin, whereas syphilis is seen to yield to the use of iodin.

Scabs in laryngitis sicca may resemble a tuberculous ulcerative process (M. Schmidt).

THROAT, EAR, NOSE.

Tuberculosis of the oral or pharyngeal cavities is a far less frequent complication of pulmonary tuberculosis, for the reasons already mentioned. The tonsils, however, are frequently affected, but give no pronounced symptoms. Tuberculosis of the pharynx, under the form of miliary tubercles or cleft-like ulcerations, generally appears toward the end of life. Dryness, dysphagia, and sometimes severe pains, which may shoot toward the ear, are the chief complaints, and are sometimes so severe that death comes as a relief. Improvement and recovery are rare. In the mouth, the tongue is the favorite seat of tuberculous ulcerations and tumors, or of lupoid vegetations. Pain, difficulty in chewing, and salivation are the chief symptoms.

In suppressed cough or cough with vomiting sputum finds its way into the nasopharynx and the nose. The adenoid tissue of the tonsils favors the localization of the bacilli in the nasopharynx, where, however, they produce slight disturbance and often pass undetected. Large ulcerations are associated with severe shooting pains and increasing dysphagia. The cervical glands are generally swollen.

Nasal tuberculosis in consumptives is not due to sputum. Its localization upon the septum and at the meatus rather points to an infection from without, most probably by the finger soiled with sputum. The patients complain of obstinate snuffling, bleeding, scabbing, interference with respiration, and nasal obstruction. Rhinoscopy reveals ulcers, tumors, or lupus. The cervical glands of the same side are often swollen. The condition is distinguished from syphilitic disease by the character of the neighboring tissues, which are normal, while in syphilis they are generally inflamed, by the preference for the cartilaginous portions, and by the absence of odor in the discharge (tubercle bacilli, tuberculin injections). Tuberculosis of the nose is in so far of importance, that the lymphatics may carry the infection into the interior of the skull, giving rise to a tuberculous meningitis.

Tuberculous otitis media often complicates a phthisis. Here, too, an important rôle is played by the sputum, which may be driven by violent cough from the nasopharynx through the Eustachian tube into the middle ear (page 162).

ESOPHAGUS, STOMACH, AND INTESTINE.

Pulmonary tuberculosis tends to infect the different parts of the intestinal tract with a varying degree of frequency. The esophagus and stomach, thanks to certain peculiar conditions, are rarely involved (pages 130 and 134).

On the other hand, tuberculosis of the intestine is an almost constant accompaniment of advanced phthisis. It displays itself in the form of tuberculous infiltrations, and of ulcerations which generally run transverse to the gut and are circular in shape. Their origin, through the voluntary or involuntary swallowing of sputum, their preference for the ileum, the ileocecal valve, the appendix, and the cecum, have been mentioned in the discussion on etiology (page 137).

Clinically, an intestinal tuberculosis often runs its course without symptoms; it may give rise to pain, which is either spontaneous, elicited by pressure, or colicky, and which is often sharply circumscribed; and to diarrhea. The diarrhea of consumptives may also be due to other causes, *e. g.*, the toxins contained in the sputum which is swallowed. Its frequency is no criterion of the occurrence of the disease, for at the autopsy of consumptives we often find very insignificant lesions of the gut in cases which presented severe diarrhea, and, vice versa, ulcerations which gave rise to no diarrhea *intra vitam.*

The latter condition is easily explained; the diarrhea depends on the position of the ulcer. According to Nothnagel, ulcers of the small intestine, cecum, and ascending colon give rise to diarrhea only in presence of other conditions, *e. g.*, catarrhal inflammation, amyloid degeneration, etc. The diarrhea is very constant, however, when the ulcers lie in the lower part of the colon or the rectum. Isolated ulcers, however, even though situated in the lower part of the colon, may not hasten peristalsis. The fact that tuberculous ulcers especially tend to select the ileum and to avoid the colon, explains the absence of diarrhea. Thus the absence of diarrhea does not exclude the diagnosis of tuberculous ulceration, and its presence does not prove it.

Diarrhea in consumptives may also be due to amyloid degeneration of the vessels in the wall of the intestine; in this case, blood in the stool and pain do not occur, and there are the symptoms referable to amyloid disease of the other viscera—liver, spleen, and kidney. In the absence of other causes, any of the following symptoms point very strongly to tuberculosis of the intestines: pus in the stool, even in small amounts, since it rarely occurs with simple catarrhs (Nothnagel); the presence of blood or hematin crystals, which may, however, be absent, owing to the obliteration of the blood-vessels; and, finally, the presence of tubercle bacilli, first demonstrated by Lichtheim, although these are occasionally derived from the sputum which has been swallowed. More upon this subject is to be found in the volume on *Diseases of the Intestines* in this system. At times, one can palpate indurated areas of the gut, or infiltrated mesenteric glands, which are often simulated, however, by fecal accumulations.

More rarely, in about 5 per cent., there are tuberculous fistulæ in one, and still more rarely, tuberculous tumors and lupus of the anal region (pages 145 and 146).

BRAIN, EYE, BONES.

Tuberculous meningitis complicates pulmonary tuberculosis most often, relatively, in childhood and youth, and brings about a fatal termination. As a rule, it is due to an invasion of the blood-stream by the bacilli, but may arise by lymphatic extension from the nose, the nasopharynx, or the ear (page 234). There are prodromata of indefinite character—disturbances of temperament, sleeplessness, twitchings, or grinding of the teeth. The course of the disease is marked by any of the following symptoms: headache, vertigo, stupor, sometimes loss of consciousness or delirium, *cri hydrocéphalique,* rigidity of the neck, retraction of the abdomen, constipation, and vomiting; eventually there are focal symptoms, paralyses, contractures, increased vasomotor irritability, and inequality of the pupils. The diagnosis may be verified by the discovery of choroidal tubercles, or of the bacilli in the cerebrospinal fluid (lumbar puncture).

The ocular complications of pulmonary tuberculosis, as a rule, occur only when the bacilli find their way into the blood-stream. They usually take the form of miliary tubercles in the choroid. Infection of the conjunctiva and cornea by the sputum carried on the finger is, on the whole, very rare (page 213). The local condition, the ophthalmoscopic picture, and, finally, the discovery of tubercles or tubercle bacilli in excised portions of tissue are the chief factors in the diagnosis.

Tuberculosis of the bones and of the joints is generally a hematogenous complication, and is also most frequent in youth.

THE GENITO-URINARY APPARATUS.

The genito-urinary apparatus is more frequently the site of secondary infections; according to von Krzywicky, in 5 per cent. The genital organs are affected more often than the uropoietic (ascending infection). The infection of the genital apparatus is by no means always hematogenous; in twenty-nine autopsies, von Krzywicky did not find one case in which this condition was due to hematogenous dissemination. Particularly if the organs between the lungs and the genitals are intact, is some other mode of infection to be thought of, notably exogenous autoinfection by the sputum, as has been explained in detail in a special chapter (page 203). This fact is the more important in that we must take prophylactic measures against its occurrence in consumptives.

Tuberculosis of the urinary organs produces the following symptoms: tenesmus, a pricking at the meatus, pain located either in the kidney region or in the bladder and shooting out over the thighs, increase of the pain in locomotion, polyuria, and, in case of occlusion of the ureters, colic and hydronephrosis. The urine is generally pale yellow in color, and often contains a great deal of pus, mucopurulent detritus, and caseous particles, blood and albumin in proportion to its content of pus and blood. Filtration diminishes the amount of albumin, unless there be a coexistent chronic nephritis. The reaction is generally acid in disease of the kidney, alkaline in disease of the bladder. The diagnosis suggested by inspection and palpation is confirmed by the demonstration of tubercle bacilli in the urine (not to be confounded with smegma bacilli), by inoculation, and, in case of the bladder, by the cystoscopic findings.

Tuberculosis of the adrenals declares itself chiefly by the pigmentation of the skin, which is at first a light or smoky gray, later becoming darker.

SKIN.

Secondary involvement of the skin is mostly in the form of lupus, more rarely tuberculous ulcerations. The latter are generally situated at the openings by which the sputum is voided, namely, the mouth and anus, and mark the advanced stages of the disease. Skin lupus is generally due to exogenous infection, which the consumptive is only too apt to induce with besmirched fingers or handkerchiefs (further page 118).

Rupture of a tuberculous focus into a blood-vessel gives rise, in case of arteries, to a miliary dissemination of tubercle bacilli in the lung itself, in case of veins to a more or less general dissemination over the entire body (disseminated miliary tuberculosis).

The different stages of development in which the hematogenous foci are found in the various organs would seem to show that the invasion, in which very often only a few bacilli take part, has repeated itself at intervals and in different vessels, so that one may speak of a series of blood-infections. As a rule, however, there is a liberal distribution of bacilli, with tubercle formation in the liver, spleen, kidney, etc., so that death precludes a second invasion.

COMPLICATIONS DUE TO THE PRODUCTS OF THE BACILLI.

In addition to the complications described above, which are due to the action of live bacilli, there are still others which are traceable to the proteins and the metabolic products of the micro-organisms and to the decomposition products of the tissues. The passages by which these products leave the body are the first to suffer, and since the mucous coating of the sputum is penetrated by the toxins more easily than by bacilli, the former are more apt to injure the tissues of the channels through which they pass.

Such complications have for the most part been already described in connection with the symptomatology. The most frequent effects of the local irritation of the toxins in the sputum are bronchitis, tracheitis, laryngitis, and pharyngitis; then gastritis (especially if much sputum be swallowed) and intestinal catarrh (pages 360, 374, 403, 404).

The absorption of the toxins into the circulating fluids is responsible for the anemia, the neuritis, and the atrophy and fatty degeneration of the muscles and heart (see "Symptomatology"). The absorption of the toxins results in still other complications—namely, the types of peritonitis, pleurisy, pericarditis, and meningitis which are not associated with tubercle formation; they are not distinguishable clinically from those of different origin.

Fatty degeneration of the liver occurs in a large proportion of consumptives; according to Frerichs, in about 68 per cent., of which 14 per cent. are severe; according to Gabler, in 10 per cent. In addition to the venous stasis of the liver and the pyrexia, it is not improbable that the action of the toxins in the blood may play some part in the production of this condition. Various writers have attributed it to the fatty diet of consumptives (?). Fatty liver, if of high grade, is marked by a feeling of tension or even pain in the liver region, anorexia, flatulence, and diarrheal stools, which are poor in bile and therefore light-colored and often malodorous. There may be a fatty condition of the skin (Frerichs). The liver is enlarged and soft.

Amyloid degeneration of the liver and of the other organs of the abdomen occurs less frequently and marks the later stages of phthisis, when there are cavities. It is also, perhaps, the direct or indirect consequence of the bacterial toxins, as is indicated by its occurrence in other forms of prolonged suppuration, as syphilis. Phthisis is the most frequent cause of this change. In 265 cases of amyloid kidney, Wagner found phthisis 136 times. The spleen is generally the first organ to enlarge; the hard, rounded border of the organ is discoverable by palpation. The liver becomes large, firm, smooth, and of a boardy hardness, whereas the fatty liver is soft; the margin is blunt. Subjectively, there is a feeling of tension in the right hypochondrium, and eventually dyspnea.

In amyloidosis of the kidney the urine is generally diminished, of a citron or reddish-yellow color, and full of albumin. Edema, hydrops, anasarca, and ascites occur. The intestinal mucosa is also often affected by amyloidosis. In connection with a similar condition of the liver, it gives rise to stools which are poor in bile, profuse, but not bloody. The complication is of importance as a factor in the disorganization of the body.

OTHER COMPLICATIONS.

Finally, dilatation and hypertrophy of the right ventricle are not rare events. They are essentially mechanical complications, and are brought about by the obstruction to the circulation in the pulmonary circuit.

The cutaneous complications of phthisis—pityriasis versicolor tabescentium, chloasma phthisicorum, herpes, which is rarer, emphysema, edema, and thrush, which is usually terminal—have already been described.

SECONDARY OR MIXED INFECTIONS.

The atypical course of pulmonary phthisis and the varying character of the fever, which differs so markedly from that of most of the other infectious diseases, very early suggested the idea that other bacteria are associated with the tubercle bacilli, and that they modify the process both by their proliferation and by the products of their metabolism and decay. The clinical fact that extensive infiltration often develops within a few days, that it disappears again completely after a time, or leaves behind caseous foci which later soften, does not seem to accord with the character of the tubercle bacillus, with the slowness of its growth, and its tendency to hold the territory which it has once won.

These considerations, as well as my observation that animals, especially rabbits, which had been inoculated with the sputum of acute phthisis often died in a few days of septicemia (before the tubercle bacilli could have come to development), led me, as early as 1888, to undertake the search for these complicating bacteria.

Koch and Gaffky had already identified the tetragonus as an occasional factor in tuberculosis, and had indicated its pathogenic value. Babes was frequently able to demonstrate that organs with tuberculous disease contained pus-cocci, the bacteria of pneumonia, and other pathogenic micro-organisms, in addition to the tubercle bacilli. I also investigated the contents of about eighty cavities, for the most part within a few hours after death, and found Streptococcus pyogenes, Staphylococcus aureus and albus, the pneumococcus, the pyocyaneus, the tetragonus, and a large number of other forms, sometimes in pure culture, and in enormous numbers. This fact, in conjunction with their pathogenic character, as determined by animal experiment, left no doubt that they were a factor in the course of phthisis. Evans determined four different bacteria of decomposition in cavities; Tschistowitsch grew Staphylococcus pyogenes aureus and three other forms from the pus of a cavity which had perforated to the exterior; Pansini had similar results.

The study of the flora of cavities was largely advanced by the method suggested by Koch and applied by Kitasato, which consisted in freeing the sputum of the accidental bacteria collected in the bronchial tree and the mouth by frequent washings in sterile water, and then growing the true bacteria of the cavities from the central portions of the sputum.

Kitasato found streptococci most often. The further researches of the author, Petruschky, C. Spengler, Schabad, and others, which also took account of the clinical phenomena, led to the same results. The streptococci were most frequent, then pyocyaneus, diplococci, tetragonus, staphylococci, the micro-organisms of influenza and pseudo-influenza. Ehret recently found numerous pseudo-diphtheria bacilli in the washed sputum of four diabetics, and Schütz in a very thorough research (thirty cases), asserts that he not infrequently found diphtheria or diphtheria-like bacilli in the washed sputum and in the bodies of non-diabetic consumptives, and that he was able to establish their pathogenic properties.

The clinical importance of the secondary bacteria is attested also by their presence in the tissues. The author and others have often succeeded in detecting them in the walls of cavities, in which they have seemed to keep pace with the tubercle bacilli, and even at times to precede them. Moreover, Streptococcus pyogenes, the staphylococcus, and the pyocyaneus have often been found in the blood, in the tissue-juices of the other viscera, and in miliary tubercles their virulence has been proved in part by animal experiment, and their pathogenic significance for the human invalid clearly evidenced (Holst, the author, Petruschky, Kossel, Pasquale, Huguenin, Jakowski, Schabad, Hirschlaff, Schütz).

The discovery of such secondary forms in miliary tubercles widely separated from the original focus, as has been described by Kossel and the author, demonstrates the intimate association of the tubercle bacilli with the other forms and the close connection of the processes which both induce, since it is evident that both species find their way simultaneously into the eroded vessels, and become deposited together in the various tissues.

Ziegler had early suspected that these secondary bacteria played a not unimportant rôle, and the same view had been expressed by Czaplewski, Maragliano, Weichselbaum, Jordan, Strümpell, and Bäumler. Bäumler refers particularly to the dissemination of the secondary forms through severe hemorrhages from the varices and aneurysms of cavities; these happen to apparently healed consumptives, and rapidly lead to death, with pyrexia and catarrhal manifestations in the finest bronchi. In such cases it is evident that a bronchopneumonia has been set up by the aspiration of the bacteria of the cavity into the healthy lung.

Moreover, we find analogous conditions in the tuberculosis of other organs. Thus, E. Fränkel has found streptococci and staphylococci in tuberculosis of the larynx. Moos emphasizes the alteration in the character of a tuberculous otitis media when it has become complicated by Staphylococcus pyogenes (great pain and rapid disorganization). Leloir, and Leloir and Tavernier, considered that the pyogenic cocci were largely responsible for the ulcerative processes in phthisis. Very probably, a mixed infection is often at the bottom of the empyema of consumptives.

I have already taken occasion in various connections (syphilis of the larynx, carcinoma of the esophagus, typhoid ulcers) to note the fact that the tubercle bacillus may also assume the rôle of a secondary bacterium, and produce definite pathological changes. Hansemann, especially, has emphasized this fact.

Clinically, a mixed infection reveals itself through fever, particularly the steep temperature curve of hectic, the character of which—pronounced morning remissions, chills and profuse sweats—recalls the septic fever of the surgeons, streptococcus fever, etc. I do not wish to intimate, however, that all fever in consumption is due to secondary infection, for even tuberculin causes fever.

These secondary bacteria, especially the pus-cocci, seem to induce rapid softening of the tissues, as is shown by Prudden's experiments on rabbits. Their presence is not necessary for cavity-formation. Only recently I observed cavity-formation, although limited in extent, in cases of pure tuberculosis induced in animals by dry inhalation.

In addition to the absorptive fever which these bacteria maintain or increase, in addition to the rapid destruction of tissue and the hemorrhages for which they are responsible, they may also give rise to acute pneumonia, in case they are aspirated into the healthy lung on their way from the cavities to the exterior. Bronchopneumonic foci arise in this manner.

The frequent absence of tubercle bacilli in these lobular foci of pulmonary tuberculosis suggested a different origin (Wesener, Davidsohn, Langerhans). Ortner, in particular, has made careful studies upon this subject; he seems to overshoot the mark, however, in making the secondary bacteria entirely responsible for these bronchopneumonias, thus neglecting the rôle of the tubercle proteins as chemical irritants. In his cases he found Micrococcus pneumoniæ most often, and regards this micro-organism as a link between Diplococcus pneumoniæ capsulatus lanceolatus and Streptococcus pyogenes.

In addition to the pneumonia described by Fränkel and Troje, which is due entirely to the proteins (pages 353, 443), there is also, then, a mixed form of pneumonia, which is caused by the combined action of the proteins and the secondary bacteria. The tubercle bacilli, which are aspirated at the same time, give evidence of their peculiar action on the tissues only after weeks, not because they need a preparation of the soil, as Biedert and Siegel assumed, but on account of the slowness of their growth. The number of foci is in direct proportion to the number of bacilli.

Finally, the secondary forms are capable of altering the type of miliary tuberculosis and of pleuritic exudates; possibly they find their way alone into the circulation, and induce the corresponding pathological changes—suppurations, hemorrhages, and purpura. The latter process affords the explanation for the cases of Babes, Etienne, and Specker.

We are not as yet in a position to differentiate clinically between the effects of the various secondary organisms.

In spite of numerous careful researches, the mixed infections are still very obscure. Various objections have been made to the previous statements. It is said that the secondary bacteria invade the walls of cavities after death, that so many different bacteria find their way into the lung that every consumptive would suffer from mixed infection, and, finally, that the presence of the so-called secondary bacteria in the sputum does not correspond with the temperatures.

As far as my own researches permit me to judge it is inadmissible to ascribe the presence of the secondary forms in the walls of cavities to post-mortem processes. I found them, in part, in bodies which were autopsied within a few hours after death, and my investigations were made in winter, a season at which the increase of bacteria is rather slow. The main objection to this interpretation, however, is the fact that the streptococci and the tubercle bacilli are about equally far advanced in the tissues—a condition which the great difference in their rate of growth renders incompatible with the post-mortem theory. Of the same significance is the occurrence of both species in miliary tubercles widely separated from the original focus.

The second objection, which is based on the notion that the deeper air-passages and the lungs are a sort of camping-ground for bacteria, is just as ill founded. The consumptive, like every one else, does, indeed, breathe in a great number of different bacteria, but the most of these are arrested in the nose, the nasopharynx, and the mouth, and only a minute fraction, perhaps a hundredth or thousandth or ten-thousandth part, reaches the trachea and the larger bronchi, and of these the barest remnant penetrates to the ultimate bronchi. And then, of the bacteria which reach this point, only a minimal proportion are pathogenic. Even these bacteria tend to be driven out of the lung again by the action of the ciliated epithelium and the *vis a tergo* of the upward stream of mucus. Their sojourn is limited, their growth is inhibited by the viscous, non-diffusible character of the medium, and the bronchial secretion very probably exerts a bactericidal or inhibitory action upon them, similar to that of the oral or the vaginal mucus. On this account the air-passages of healthy animals, if properly examined, are always found sterile.

The last and most important objection, namely, the lack of parallelism between the condition of the sputum and the temperature curve, collapses if we take account of the course of a mixed infection. Only caseous areas and cavities are to be considered as affording an opportunity of development to the secondary forms, since the bacteria are undoubtedly carried past solitary tubercles in the bronchi by the current of secretions.

The caseous focus is in relatively slight danger from secondary forms, unless, indeed, they originally took part in its development. Such a focus does not breathe, so that there is no inspiratory current to carry along the bacteria. They may, however, find their way to it, either by being projected from a neighboring area or through a patent afferent bronchus.

The consequences of such an invasion depend upon the character of the bacteria. Streptococcus and Staphylococcus pyogenes, which cause suppuration and destruction in healthy tissues with an accompanying febrile movement, will certainly find full play for their activity in the injured and necrotic tissues.

Cavities whose walls dilate in response to the inspiratory tension at the surface of the lung are certainly in far greater danger. The influence of the secondary bacteria upon the course of the phthisis depends not only upon the character of the micro-organisms, but also upon the condition of the cavity-wall. The ordinary saprophytes, which are the most frequent invaders, have no clinical significance.* But even true pathogenic bacteria may find their way to a cavity and develop there, without giving the symptoms of a mixed infection.

The cavity is no longer an integral part of the body. In the first place, the cheesy matter which often lines the wall of the cavity in considerable quantities offers a certain hindrance both to the invasion of the secondary bacteria and to the diffusion of the secondary toxins. In the second place, the wall is often indurated, and is then almost or absolutely impermeable both to the tubercle bacilli and the secondary forms and their toxins. In sections of the walls of such cavities, I found that the inner zone contained a number of tubercle bacilli and of secondary forms, but that the chief part of the wall, the connective-tissue layers, was absolutely devoid of any. Spengler describes similar findings. The bacteria probably perish within a short time in these closed cavities, just as they do on dead media; they are then gradually eliminated, and for once the cycle of objective changes has run its course without giving rise to any clinical symptoms.

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* We are unable to say whether they diminish or intensify the effect of the pathogenic bacteria already present.

In such cases the bacteriological examination of the sputum reveals pathogenic and virulent bacteria, even in the absence of fever. This does not, however, constitute an objection to the theory of mixed infections. The only danger from cavities of this kind is that the sputum may give rise to aspiration pneumonias on its way to the exterior.

If the tissues of the cavity-wall are only slightly indurated, the proteins of the secondary bacteria, as well as those of the tubercle bacilli, penetrate into the tissues, are taken up by the circulating juices, and produce fever and other symptoms. Increase of the hydrostatic pressure, either by blocking of the secretions or by violent coughing, tends to force greater quantities of the toxins into the peripheral tissues.

The process does not stop with the absorption of the diffusible proteins, but the bacteria themselves invade the cavity-wall, if it be well supplied with lymph-spaces, and induce suppuration and rapid destruction of the tissues. This fact is clearly demonstrated by the histological picture. But even in this case the greater portion of the bacteria and their poisons are carried to the exterior, and may set up an aspiration pneumonia on their way.

It is very important to remember that the colonization of one cavity by pathogenic bacteria does not put the imprint of a mixed infection upon the entire tuberculous process, with all its different foci and cavities; for the secretion of the cavity which has been secondarily infected is enveloped in the mucus of the bronchi through which it passes on its way to the exterior, and does not come into contact with other parts of the lung except at the intersections of the bronchi. Thus, there may be an offensive mixed infection in one cavity, while the next cavity remains free from the infection through its entire course, or contains only the usual horde of saprophytes. Indeed, the various balls of sputum often show a very different appearance macroscopically.

This fact, which I emphasized in connection with my earliest investigations upon the cadaver, and which received confirmation from the striking demonstrations of Hansemann (see Bibliography), is easily overlooked by those who confine themselves to an examination of the sputum *intra vitam.* In invalids of this kind the results of an examination of the sputum vary according to the origin of the different particles which are selected, and in spite of high fever one may discover only harmless or slightly virulent parasites. The danger of confusion is enhanced by the fact that streptococci are chiefly in question, and that these may be of a virulent variety in one cavity and innocuous in another, so that it is merely a matter of chance whether one selects the real culprit for experimental inoculation.

The presence of secondary bacteria cannot be determined from a few examinations. Personally, I have often made as many as eighteen examinations in one case, before I could come to a definite conclusion. The results of Schroeder and Mennes, which seem to speak against mixed infections, are invalidated by just these fallacies in their procedure. Moreover, there may be extensive streptococcus-invasions of the lung with an almost afebrile course (Spengler and Wassermann).

The examination for secondary bacteria is conducted in the following fashion: The patient washes out his mouth with boiled water, and then voids the (morning) sputum into a sterile Petri dish. Several of the sputum-balls are then isolated, in so far as their consistency permits of this, and each of them is then thoroughly stirred about in six to ten dishes containing freshly boiled water. Finally, a small piece is taken from the center of each particle and smeared over the surface of gelatin and glycerin-agar (perhaps even serum-glucose-agar or blood-agar), and grown at a temperature of about 37° C. for sixteen to twenty-four hours, except the gelatin, which is grown at room-temperature. The rest of the sputum is examined microscopically.

In case similar colonies grow in large numbers upon the media, one determines their biological characteristics, *i. e.*, isolates and identifies them. Single colonies of a species may be neglected, as they can hardly indicate a mixed infection.

Their pathogenic properties are tested by injection of the cultures subcutaneously, in as fresh condition as possible, into the ear of rabbits, or intraperitoneally in rabbits, mice, or guinea-pigs. Inasmuch as the virulence may become attenuated by artificial cultivation, and, further, the combination of different species in one cavity may alter the activity of the individual forms, it is advisable to institute control experiments with fresh washed sputum. If the case comes to autopsy, one should control the clinical findings by making smears, sections, and cultures from the various foci and cavities.

Secondary infections are not always followed by untoward consequences. Under exceptional circumstances, as when they occupy the periphery of tubercular foci, they may reinforce the irritant influence of the diffusible proteins upon the capsule and so serve to limit the dissemination of the tubercle bacilli. In this way I would explain certain observations, such as the fact that lupus was temporarily improved by Streptococcus erysipelatis (Bertarelli, Winternitz, Kollath, Isnardi, Hallopeau), and that pulmonary tuberculosis was brought to a halt or to recovery by erysipelas (Waibel, Schäfer, Chelmonski—who also reports a cure through typhus).

Inoculation with virulent erysipelas, a therapeutic application which has been suggested and even practised, I cannot indorse; one is in the same peril as the apprentice in magic, who cried: "The spirits which I have invoked, I cannot now escape."

CHAPTER VI.

PROGNOSIS.

It is a difficult task to make even an approximate prognosis in consumption. We are called to an invalid who has for a long time had considerable fever, and who bears indubitable marks of extensive tuberculous infiltrations. He loses the fever, gains in weight, and, to our astonishment, may be in good health for years.

Eleven years ago I treated a colleague who had fever of 40° C. (104° F.), dulness on the right side to the fourth rib, behind and in front, and on the left side to the second rib, and who was brutally forced out of his hotel because his death was momentarily expected. To-day he has a large and arduous practice, is married, and considers himself cured.

In other cases the symptoms of phthisis have so far receded that we consider the case cured. The patient is blooming and healthy. Of a sudden comes an hemoptysis, fever and bronchopneumonia succeed it, and in eight to fourteen days the man is dead. Nevertheless, there are certain cardinal points which may be taken as guides in prognosis. General considerations are of importance.

The prognosis depends upon the strength of the patient. Persons who have been weak from youth, their parents having been sick at the time of conception, either with lues, tuberculosis, cancer, or any other severe disease; persons who are weakened by past or present illness, typhoid, syphilis, anemia, or diabetes, or by loose living, excesses *in Baccho et Venere*, or by severe mental or bodily exertion, and women after frequent lying-in or lactation, all these offer a poor prognosis, especially if there is much disturbance of nutrition. The younger the patient, the worse the prognosis; only after the sixtieth to the seventieth year, when the fat has become atrophic, does the prognosis again become worse.

The financial condition of the patient is of great importance. The increased demand for food, the prolonged treatment, the enforced idleness, the lengthy sojourns in selected places, require great material resources. Yet we must not despair of the less fortunate; our autopsies demonstrate daily the possibility of cure.

The character of the patient is of great importance. If he cannot regulate his habits, control his passions, and accustom himself to a fixed mode of life, if he is indolent, flighty, dissolute, or weak, he offers a far worse prognosis than does one who is firm and collected. Cheerfulness is vastly better than depression. The saying that a man dies of his disposition rather than of his disease has a particularly just application in phthisis.

The degree of intelligence is also of importance, for the prolonged course of the disease makes certain demands upon the intellect to recognize and avoid injurious influences, even though the physician be not present to guide.

The condition of the digestive tract is of critical importance. A good appetite and a healthy digestion are of inestimable value in seconding our efforts. Even the normal processes of nutrition and fat-formation suffer from disturbances of digestion. How much less fitted is a weak digestion to offset the pathological deficiency of consumptives? Bankruptcy of the body will come only the more rapidly, especially if diarrheas increase the deficit.

As regards the disease itself, the physical examination does not always give a reliable clue to the prognosis. The miliary type, which is the most dangerous, is at the same time the most easily overlooked. On the whole, the previous course of the disease is more significant than its extent. The presence of cavities of even considerable size does not exclude improvement and cure, if only fever, emaciation, and signs of progression be absent.

The more extensive the foci, the worse the prognosis. It is most favorable if the process is limited to one apex. The prospect of recovery is seriously impaired by involvement of the opposite apex, and by the signs of the destruction of tissues or of rapidly progressing infiltration; *i. e.*, of a bronchopneumonia. Whether this is a resolving process, induced by the proteins and the secondary bacteria, or a true tuberculous affection, we have still to learn.

Very great importance attaches to the fever. Apyrexia, if accurately determined, is almost always a sign of quiescence, and quiescence (with the exceptions noted on page 387) denotes the beginning of recovery. On the other hand, even a slight fever, with evening rises no higher than 37.7° C. or 37.8° C. (99.8° or 100° F.), makes me anxious for the future of the patient. These exacerbations are an indication that he is on the downward course, and no one can tell where this will find a halt. Higher fever is, of course, still more serious; but still more unfavorable are the steep curves with remissions to a subnormal, collapse temperature or *febris continua*, which often brings the disease to a rapid close. Sweats have a similar prognostic significance.

Progressive emaciation is always to be regarded with the greatest anxiety, since it is not only a symptom of disorganization, but contributes directly to the extension of the disease (see page 407). A steady equilibrium or increase of weight, if not due to edema, is an auspicious sign.

Cough in itself has but little bearing on the prognosis. But the indirect effects of cough—the exhaustion, the night-sweats, the vomiting, the hemorrhages, and the aspiration—always make it a factor in the result. The same holds true of expectoration. Abundant sputum does not necessarily arise from the process in the lung, but injures the organism by depleting the body-juices. A small amount of sputum does not in itself justify a favorable prognosis, for the most dreaded form of the disease, the miliary type, has no influence upon the quantity. Yet it is a favorable indication if a sputum which has been profuse and purulent diminishes in amount and comes to contain fewer formed elements.

The number of the bacilli furnishes no reliable criterion for the prognosis. Rapidly softening foci throw off enormous numbers of bacilli; the dangerous miliary foci, on the other hand, throw off none at all. In general it is satisfactory if the number slowly diminishes, and if the eventual disappearance of the bacilli can be confirmed by repeated examinations. The absence of pathogenic secondary forms is also a favorable sign.

Traces of blood in the sputum, small hemorrhages of two or three dessert-spoonfuls, are in themselves of no moment. They are dreaded more than they deserve to be. Indeed, they are often in so far of value that the patient grasps the dangers of the disease, and takes corresponding care of himself. In some cases they lead to a serious depression of spirits.

Profuse hemorrhages often denote a turn for the worse. The anemia is increased, and blood mingled with sputum is very apt to be aspirated into healthy territory, setting up pneumonia and caseation. Death even may result from suffocation and acute anemia. Tachycardia (even without fever), dyspnea, and sleeplessness, are to be interpreted in the same manner.

Prognostic significance is also attached to the second pulmonary tone: pronounced accentuation argues that the right ventricle is powerfully combating the obstruction in the pulmonary circuit;

decrease of an existing accentuation with moderate dyspnea argues an easing-up of the lesser circulation, while its association with increasing dyspnea indicates exhaustion on the part of the right ventricle (Smith).

Of the complications, tuberculosis of the larynx or intestine is of especially evil import, but not so hopeless as it was once considered, for spontaneous recovery may take place in either organ, and well-timed interference in case of the larynx often checks the process. Pharyngeal tuberculosis may be regarded as a practically fatal complication, on account of the associated dysphagia. Pleuritic exudate and pneumothorax may induce momentary improvement, but in the long run hasten death.

[Spengler* has reported four cases of pneumothorax complicating pulmonary tuberculosis, all of which went on to the cure not only of the pneumothorax itself, but also of the tuberculosis. He considers the outlook in this condition comparatively good if the exudate is serous or sero-purulent, without a secondary pyogenic infection. Such a favorable outcome of this complication, however, is not in accord with the experience of most physicians.—Ed.]

In short, every extension-tuberculosis of the pericardium, bones, joints, etc.,—especially meningeal tuberculosis,—is of evil import.

Edema, as the sign of degeneration of the heart and of amyloid disease, is to be regarded as a prodrome of early or even imminent death. Thrush, too, is generally terminal. (Concerning the diazo reaction as a prognostic feature, see page 409.)

On the whole, the prognosis of pulmonary tuberculosis is to be regarded as serious, but by no means absolutely unfavorable. It would be still more favorable if the patient would seek the physician earlier, in the case of obstinate catarrhs, etc., if the physician did not frequently permit himself to be led astray by the excellent family history and the healthy appearance of the patient, and if the necessary measures were energetically enforced.

[The conclusions of various observers regarding the value of the diazo reaction in the prognosis of pulmonary tuberculosis differ.

Michaelis,† Blad and Videbeck,‡ agree that a pronounced diazo reaction makes the prognosis bad.

Giesler§ concludes that it is not a constant accompaniment of most cases even in the advanced stage, and hence that it is of very limited prognostic value.

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* Zeitsch. f. Tuberc. u. Heilst., Bd. ii, 1901.

† Deut. med. Woch., 1899.

‡ Zeitsch. f. Tuberc. u. Heilst., 1901, p. 412.

§ Zeitsch. f. Tuberc. u. Heilst., 1902, p. 406.

Wood* studied 663 cases of pulmonary tuberculosis, and concludes that if the urine shows no diazo reaction, and a kidney lesion may be excluded, then the prognosis is good. If it shows a continuous, well-marked reaction, the prognosis is bad.

It is evident from the above, which may be taken as a fair example of the contradictory reports that have been given, that the procedure is of no real practical value. In advanced cases of pulmonary tuberculosis, there are many other clinical phenomena which will give a clearer clue to the outlook.

Teichmüller has stated that the presence of eosinophiles in the sputum was a good prognostic indication, and pointed to a favorable termination.

Pelnar,† on the contrary, finds no relation between these cells and the number of bacilli, the stage or the severity of the disease. He finds that many eosinophiles rather point to the presence of some complicating inflammation, such as bronchitis, and says that they have no bearing upon either prognosis or diagnosis.—Ed.]

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[*] Med. News, 1903, p. 631.

[†] Rev. Zeit. f. Tuberc. u. Heilst., 1901, p. 539.

CHAPTER VII.

PROPHYLAXIS.

The battle against tuberculosis rests for the most part upon our knowledge that the causal agent is the tubercle bacillus. Out of this knowledge arise certain definite indications. We must attempt: (1) to annihilate the organism, to limit its spread, and to prevent its entrance into the body; and (2) when it has once gained entrance, to eliminate it as quickly as possible, or to circumscribe its growth, by means of the vital energies.

The first of these indications constitutes the goal of our so-called antibacillary prophylaxis; the second, that of our individual prophylaxis and in part of our therapeutics.

ANTIBACILLARY PROPHYLAXIS.

Antibacillary prophylaxis, as has been shown more in detail in the etiological sections of this book, is based upon the following conditions.

The tubercle bacillus is an obligative parasite, *i. e.*, it is unable, under natural conditions, to increase outside of the animal body, partly because it demands high temperatures, and partly because its slow growth permits the omnipresent saprophytes to crowd it out of existence. It finds its way into the environment of mankind only as part of the secretions and excretions of tuberculous individuals, and in the meat and milk of infected animals.

As we saw in the section on infection, the usual routes are as follows: the inhalation of air containing bacilli, the use of infected food, and direct contact in cases where the bacilli come into contact with wounds or abrasions of the skin and external mucosæ.

The last form is of the least importance; cleanliness suffices for avoiding it. Infection through food is to be combated by cooking the food, by supervision of the slaughter-houses, and by inspection of cows. By far the greatest danger lies in the inhalation of the dried and pulverized sputum. The dissemination of tubercle bacilli through dried feces, through pus from superficial foci, and through particles which are voided in coughing, is hardly to be considered in comparison with the enormous number of bacilli voided in the sputum. The air of expiration of consumptives is sterile and harmless.

Such sputum-dust—*i. e.*, tubercle bacilli—is, as a rule, to be found in an amount and a condition which make it dangerous, only in places occupied by consumptives who are careless in the disposal of their sputum. The greatest danger is in closed places. In the open, the bacilli are usually rapidly destroyed by sunlight, distributed in the air, and rendered harmless by meteorological agencies, such as moisture, etc. The tubercle bacillus is, therefore, not ubiquitous.

The first object of the struggle against infection by the respiratory tract must be the care of the sputum. It must not be permitted to dry up, but should be kept **moist,** removed, and destroyed. In so far as this is accomplished, the danger of infection for the immediate environment is diminished, or even eliminated.

The conditions of infection and the comparatively limited distribution of the infectious material make the execution of prophylactic measures dependent essentially upon the consumptive and his immediate environment, since he has it in his power to dispose of his infectious secretions and to render them harmless to a degree not paralleled in any of the other infectious diseases (*e. g.*, cholera or typhoid). For the healthy individual, the task of avoiding tuberculous infection is more difficult, but by no means impossible.

In all cases in which the individual is unable to guard himself against infection, and in which he is menaced by tuberculosis despite his efforts to avoid it, it is the business of the state to intervene if the disease, which is really a national evil, is really to be restricted. That governmental intervention is to the interest of the state, follows necessarily from the politico-economic importance of the disease.

INTEREST OF THE STATE IN PROPHYLAXIS.

In Prussia alone the deaths from tuberculosis during the twenty years from 1875 to 1894 amounted to 1,669,587 persons, which is equivalent to the entire population of Berlin, or about 80,000 a year; in Austria, from 1881 to 1892, 1,059,300, or about 90,000 a year, of whom the majority, about five-sevenths, were bread-winners between the ages of fifteen and sixty. It is not, as, for example, in diphtheria,* a question of children, for whom the outlay has been slight, but of adults, who have not yet begun or not yet completed the task of converting this outlay into capital, so that their deaths denote a loss in national wealth.

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* Of those dying of diphtheria, about 72 per cent. are under five years of age, about 94 per cent. under ten years.

The fact that tuberculosis selects its victims just at the most productive periods of their lives, and that it conducts a campaign not of a few days, like the most dreaded forms of infectious disease, *e. g.*, cholera and typhoid, but of prolonged duration, is of importance from various points of view. It has been calculated (page 19) that the loss through tuberculosis, from the simple incapacitation of wage-earners, not counting the expenditure for physicians, nursing, medicine, and burial, amounts to more than 43 millions of marks every year in Prussia. In addition to this, there is the enormous expenditure which is entailed by the treatment of these patients in the public institutions. The number of cases of consumption and hemoptysis treated in such institutions in Prussia, during the year 1894, for example, amounted to 18,493; in Austria, to 20,508. These numbers repeat themselves year after year. An accurate estimate of the expense is impossible in the absence of data regarding the number of days of treatment. We know that in the Prussian army in the years 1874 to 1893 about one and a half million days of treatment fell to the account of tuberculosis. The yearly cost of such treatment to the state and the community is hard to conceive. The sick-funds are incapacitated for the performance of other social obligations—lengthening the period of support, etc.—through the fact that their capital is almost entirely swallowed up by tuberculosis. Further, according to the report of the insurance commissioner for 1898 of 151,083 recipients of money, tuberculosis was the cause of invalidism in 18,212, or 12 per cent. The indirect loss, through the diminution in the number of tax-payers and the increase in the demands on the pension-roll, cannot be computed.

What an amount of pain and distress, of social misery, is due to the fact that families, having lost their support, sink into pauperism, and eventually fall back upon the charity of the community! And aside from the monetary question, what an amount of moral undoing and wrong is visited upon society through the fact that children have been robbed of their mother and of the educative influence of home! Look at the orphan asylums, how many of their inmates have lost their parents through tuberculosis!

The bare loss of life through tuberculosis exceeds that contributed by war and other plagues. In the Franco-Prussian war, according to Prussian statistics, the number of men killed and dying of wounds and disease amounted to 40,951; twice as many die of tuberculosis every year. In the forty years from 1831 to 1870 about 344,000 men died of cholera in Prussia, or less than a fifth part of those dying in half that time from tuberculosis.

The defensive powers of a country are considerably curtailed. The full extent of this factor cannot be accurately gauged, since the published figures include only those taken sick during the term of service, but not those excluded from even entering it. Finally, even if a determining influence be denied to heredity, it can hardly be questioned that the descendants of the tuberculous often bear the signs of weakness, and of imperfect powers of resistance and performance (see page 324).

What a loss of property, what an inroad upon the prosperity of the farmers, is due to the devastation of the cattle by tuberculosis!

In the year 1893, for example, according to the report of the public slaughter-houses in Prussia, of 695,852 adult cattle, 62,312, or 8 per cent., were tuberculous; and of these, a great part had to be thrown away as useless. In the Berlin slaughter-house alone, from 1883 to 1892, 56,000 tuberculous swine were slaughtered.

What an enormous sum of money passes to foreign countries in order that this deficiency in the meat-supply, due to tuberculosis, may be made good—only to be replaced in great part by importations of tuberculous cattle! In 1894, 115 million of marks worth of cattle, deducting the exports, were imported into Germany, an amount which could be greatly lowered.

Tuberculosis among cattle has become an international calamity, and its limitation a burning international question.

The interests of the state are therefore most nearly touched by tuberculosis; and it is the right and duty of the state to intervene. This duty it has amply performed in the case of other important infectious diseases, such as cholera, but it has not sufficiently comprehended the truth that tuberculosis is the most destructive of all the plagues, although certain states have made a beginning in this direction.

PRIVATE PROPHYLAXIS.

With a little good-will, private prophylaxis is not very difficult to maintain. Physicians should, therefore, work indefatigably in the interests of hygiene. We should constantly remind the consumptive of the danger of his sputum for others, and of the necessity for guarding against this. It is not sufficient, however, to enforce these measures only in case of manifestly tuberculous individuals, for the infected sputum of the early and obscure stages would then be overlooked. Moreover, there is no doubt that the expectoration in certain other diseases—pneumonia, diphtheria, influenza, pertussis, etc.—contains infectious germs, which are a menace to the environment. I may here refer to the case of Mosler, cited below. Further, the universal enforcement of the rule deprives it of its sting for the consumptive. Drying of the sputum occurs most easily, according to my investigations, when it is voided on the floor or into a handkerchief, and we should therefore see to it that the patient **always spits into a vessel containing water.** If this rule is followed, we may assure the patient that he is not a source of danger to his environment.

The recent assertion of Flügge, that infection is brought about by the minute particles of sputum thrown out by coughing, is open to a number of objections. Flügge's doubts concerning the possibility of infection by means of dried sputum have been disposed of by my experiments (cited page 101). Consequently very slight importance need be attached to the particles of sputum thrown out by coughing, since the bacilli therein contained are but a very minute fraction of the number which are cast off in the bulk of the sputum and permitted to dry. Moreover, these particles are for the most part not sputum at all, but sterile saliva, as I demonstrated in another set of experiments (see page 254). When Flügge takes cultures of the prodigiosus into his mouth, determines that the germs are distributed in talking and coughing, and from this argues that the same occurs in the case of the tubercle bacilli, he neglects the most important link in his evidence, the *tertium comparationis*, namely, the proof that the saliva of consumptives contains anything like the same number of germs as when the mouth is filled with a culture of prodigiosus. Researches upon this subject show that the saliva is either free from the bacilli or contains them in rare cases and in small numbers.

Real tuberculous sputum, as has been shown, is enveloped in a mantle of viscid bronchial mucus, and this, together with the consistency of the sputum, tends to prevent the dissemination of the bacilli in the mouth; hence the rarity of oral tuberculosis. Flügge observed a sprinkling of fine droplets into the air, when drops were allowed to fall upon solid or fluid surfaces; this fact, however, admits of no comparison with viscous sputum.

The best proof that infection by droplets plays a rôle of no importance is the fact that I have never been able to discover tubercle bacilli on the walls, or otherwise distributed, in the case of consumptives who were careful with their sputum, in spite of the fact that there was ample opportunity for the dissemination of droplets. On the other hand, the results were always positive in cases in which the patients permitted their sputum to dry.

A recent research of B. Fränkel's demonstrates that the dissemination of bacilli by coughing is insignificant in comparison with the number liberated by the drying of sputum. He let a number of consumptives wear masks for twenty-four hours at a time, and with 219 of these masks he caught 2600 tubercle bacilli in thirty-two days; how many of these were viable is unknown—probably, according to Kitasato's findings, only a small fraction. Heller reckons 300 million germs to a single pellet of sputum, or 7200 millions in one day, if the patient expectorates only once an hour. On the one hand, we have a number of consumptives, thirty-two days, and **2600** bacilli; on the other, one consumptive, a single day, and **7,200,000,000**—*i. e.*, **more than two million times as many.**

Not only are Flügge's objections thus disposed of, but also Fränkel's suggestion that consumptives should wear masks day and night—a suggestion the impracticability of which is sufficiently evident. Many other considerations, such as the menace to the invalid himself, the publicity, etc., I need hardly mention; I would only recall the insuperable objections which are made by laborers in certain exposed callings to the wearing of such masks.

In order to avoid the rather insignificant danger from cough, it suffices to follow the injunction given in my first work: "At the time of sudden cough, the consumptive should hold a cloth before his mouth, so as to secure as rapid a fixation as possible of the finely divided moisture, harmless though it generally is, and that he should have the cloth cleaned as quickly as possible."

Special attention should be paid to the form and to the content of the spit-cups.

The bottom of the spit-cup should be larger than the mouth in order to avoid spilling. It should be at least 6 cm. high and with a mouth which is not so small as to demand accurate marksmanship on the part of the patient. The best place for it is a corner, because there is slighter chance of accidental infection of the clothes by contact. I always come back to the simple porcelain or enameled spittoons, which may be covered with a perforated top, so as to prevent the contents from being licked up by dogs. The objection that frequent use renders them anything but beautiful is actually an advantage, inasmuch as they demand repeated cleansing.

Filling the spittoons with sand, sawdust, or the wood-wool recommended by Prausnitz is not advisable, both because it favors dissemination and because the final disposal of these materials, either by removal or by burning, is not so thorough as simply emptying the spittoon into the privy.

It is just as great a mistake to fill the spittoons with water, as is so generally advised, since this leads to spattering. I have expressly stated that, in order to facilitate cleansing, only the bottom of the spittoons should be filled with water.

The safe and thorough disposal of the sputum is possible only if the spittoons are liberally distributed wherever the consumptive finds his way, and if they render expectoration convenient and inconspicuous. They should be placed not only in every room, but in corridors, closets, and workrooms, etc., and especially on staircases, because climbing stimulates expectoration. No house should lack them, neither the palace nor the hovel; it is folly to object that there is no consumptive among the inmates. For, in the first place, the disease is often not recognizable, and, secondly, visitors to the house may easily be tuberculous. Finally, the spittoon is designed not only for tuberculous sputum, but for any infectious expectoration, *e. g.*, that of diphtheria or influenza.

For ambulatory cases Dettweiler's sputum cup is advisable, since it serves, in spite of many shortcomings, to dispose of the sputum harmlessly. Pocket spittoons in the shape of cigar-boxes, lunch-boxes, and other devices which have been brought to my attention, have not the proper construction. All invalids ought properly to have a portable spit-cup with a cover, while for those confined to bed this is an absolute necessity.

Spittoons should be emptied in the privy, which should then be flushed out with hot water; the tubercle bacilli perish in putrefying masses. In hospitals, which have to deal with large amounts of sputum, disinfection is absolutely necessary, and is best accomplished by heat in one of the apparatus of Kirchner and Heim. Chemical disinfection, as has been already shown, is inadvisable, on account of the cost, the inconvenience, the odor (carbolic acid), and the inefficiency (corrosive sublimate). The same care must be taken with tuberculous pus and soiled dressings, which it is best to burn.

The linen and bedding are to be changed as often as possible, especially if soiled. Blankets should have washable covers. The cleansing of featherbeds, as practised in the establishments for that purpose, is not satisfactory.

It is well known that I object to the use of pocket-handkerchiefs for sputum. According to my experience, bacilli are found in the immediate environment of consumptives only in case they make use of handkerchiefs or spit on the floor, and never under other conditions. Very soon after my first communication, Mosler described an infectious pneumonia in a family, and stated that the family had constantly voided their sputum into handkerchiefs.

In order to remove remnants of sputum from the lips, and also as a shield in coughing, it is well to use handkerchiefs of Japan paper, which are to be burnt or thrown into a slop-pail as quickly as possible.

Kissing on the mouth is to be avoided.

The rooms are to be mopped up moist, since dry dusting seriously increases the danger. Immediately after cleaning the rooms are to be well aired, so as to remove the dust as fast as possible. Dust is doubly dangerous to the sick, on account of the pus cocci, etc., which it carries (secondary infection).

The atmosphere should be kept moist by exposing water in trays or by spraying, both for the favorable effect on expectoration and to prevent the dissemination of dust. Heavy curtains are to be avoided, and the sun should be given every chance to exercise its bactericidal action.

If one fears that he is in a room infected by sputum, *e. g.*, in a hotel, he should be careful to breathe entirely through the nose. He should keep out of it during cleaning and for some time afterward, knowing that it takes one to two hours for the dust to settle.

A new home should be thoroughly cleansed before occupation.

After the death of a consumptive there should be a thorough disinfection, for those in the last stages are, as a rule, too weak to observe the ordinary rules of cleanliness. The walls should be rubbed with bread, the floors washed, and the beds, pillows, linen, covers, carpets, curtains, and clothes (except furs and leather) are to be disinfected in live steam. Cushioned furniture should be beaten in the open air, and wooden furniture is to be rubbed with a moist cloth, preferably with alcohol. It would be well to cleanse the living rooms of the patient in the same way as often as possible, say, once in four weeks.

Not only his consideration for others, but his own interests, demand that the consumptive should be careful. For he lives at the center, as it were, of the infectious circle which he creates, and so imperils himself more than any other by his sputum; he really commits a slow suicide.

A priori, one might think it of slight importance whether a consumptive whose lung already contains millions of bacteria breathes in a few more or not. A careful consideration of the nature of tuberculous infection brings us to a different conclusion. In cholera or typhoid, in which the whole gut is full of bacteria, it may, indeed, be of no consequence whether a few more are taken up with the food; in scarlet fever, variola, and syphilis, in which the entire blood is infected, a few more may be disregarded. But tuberculosis is a sharply localized disease, in which every fresh infection is of consequence. Nor can the inspired germs be compared with those in the sputum, since the latter are destined to pass outward. If, indeed, the fresh germs were to find their way to a cavity or a caseous focus, their arrival would not alter matters. But, as a rule, it is the healthy tissue and not the caseous focus which aspirates. When a bacillus finds its way into a healthy alveolus, a newly formed tubercle becomes the center of a fresh infection, and this is just as serious a matter as if the gut or some other organ had become involved. *The fallacy itself and the resultant policy of inaction should, therefore, be energetically opposed.*

Above all, in order to avoid an intestinal infection, the patients should be admonished not to swallow their sputum. They might even wash out their mouths before eating, in order that no stray remnants of sputum may be carried down to the stomach.

If the consumptive persists in neglecting the welfare of his neighbors, they should take the proper measures to protect themselves, such as giving him notice to leave or isolating him. The hardship is his own doing: *volenti non fit injuria.* To notify the authorities of such dangerous persons, or even to confine them in institutions, is just as proper as in the case of cholera, leprosy, or the other infectious diseases. Personal liberty is to be sacrificed to the general good. The inhumanity, if such there be, is rather to be charged to him who makes such measures a necessity.

The following case may be cited by way of example: A consumptive (a locksmith) lay sick at home, and passed the time by seeing how high on the wall he could spit. His death was followed in a few weeks by that of his wife and child, who both succumbed to tuberculosis.

STATE REGULATIONS
AGAINST HUMAN TUBERCULOSIS.

It is the part of the state to undertake measures both against human and animal tuberculosis. It is only by means of this double battle that any sort of success can be achieved.

As regards human tuberculosis, the state should intervene in cases where the individual cannot or will not take measures against the infection. The supervision of the state should be directed to the following points:

1. In all institutions under the direction or the supervision of the state—institutes, schools, seminaries, orphan asylums, prisons, asylums, court-houses, post-offices, public rooms, libraries, waiting-rooms, railroads (especially those running to the health resorts), etc.—there should be spittoons of proper shape and in sufficient quantity, in order that both the officials and the public, which will necessarily comprise a large number of consumptives, may properly dispose of their sputum. Otherwise, they are compelled to disseminate the infectious material.

This simple indication is even to-day not nearly fulfilled, although the way was pointed out more than ten years ago. More stringent measures are needed, especially in the hospitals and in the higher and lower grades of the institutions for consumptives.

Only recently I saw six balls of sputum in the corridor of a large hospital, a fact which was explained by the scarcity of spittoons. Upon the street, esthetic principles, if no others, demand that men should spit in the gutters.

2. The right which the state long ago assumed of protecting the workmen in certain professions against the dangers associated therewith, and of exercising hygienic supervision over the factories, ought rightly to include protection against tuberculosis, and that not only in the larger factories but also in the workshops.

How often have my investigations revealed conditions such as that workshops containing as many as 50 laborers, some of whom were tuberculous, had not a single spittoon, so that the men were simply unable to dispose properly of their sputum.

A second set of conditions over which the state should exercise supervision are the lighting, the ventilation, the control of the dust, and the manner of cleansing. The cleaning should be done with mops, and should be timed so as to come not before occupation, but after it (*i. e.*, in the evening, for factories, offices, and schools, and in the morning for sleeping-rooms), in order that the dust may not be a source of danger to those using the rooms.

Control might be exercised through the factory inspectors, who could give a yearly report upon the observance of the regulations. Increase of the number of officials and of expense to the state are of no consequence, in comparison with the enormous loss which is entailed through tuberculosis.

3. In the same way, it is the duty of the state to demand suitable provision for the harmless disposal of sputum in all public places and inns. If the municipality has the right to regulate the cleansing of glasses and of the beer apparatus, the hours of business for saloons, the closet arrangements, the height of the rooms, etc., it is certainly its right in far higher degree, as well as its duty, to regulate the disposal of the infectious material of the most widespread of all contagions. This control is to be correlated with the execution of the other state regulations.

The same arguments apply to the supervision of hotels and of the miserable lodging-houses, which is in many ways more important than the official enactments concerning the minimum of cubic air space.

4. Such regulations are even more important for the health resorts and for certain summer resorts, the latter being as popular with ambulatory consumptives as the former.

5. Disinfection should be made feasible by the purchase of the necessary apparatus, possibly of a movable machine for the use of several smaller communities, and its performance should be insured through the local police regulations.

It is of especial importance that the clothes of consumptives should not be used, sold, or given away, without previous disinfection, although we need hardly demand, as in Naples or Vienna, that they should be burned.

6. Successful prophylaxis against tuberculosis depends largely on the regulations governing the lighting of houses, the height of the stories, the water-supply, the width of the courts and the streets, etc., for light, air, and cleanliness are our very best allies.

The state or community should also take measures to insure the proper cleaning and sprinkling of the streets. In this respect, conditions are most deplorable in many of the health resorts, especially in the south of Europe.

7. Concerning the supervision of the dairies, slaughter-houses, etc., see below.

8. The state should attend to the isolation of consumptives in the hospitals, as far as practicable, and should encourage the building of invalid establishments as needed, since these are important factors in combating the disease. The servants of the state when afflicted with the disease should be housed in these institutions, and in this manner the pension list might be lowered.

9. The sputum of suspicious cases among the poor should be ex-

amined at the request of the attending physician in the proper institutions, and at the expense of the state or of the community, since early diagnosis is of importance from the standpoint of both therapeutics and prophylaxis.

Not only the state, but every smaller community also, should frame regulations in accordance with its powers concerning the schools, police-stations, official buildings, etc.

The measures above suggested are undoubtedly important and necessary, one as much as the other, but those are especially indispensable in which the state sets the example to the individual, or exercises compulsion where the individual fails to live up to his duty.

Instruction.—Little is achieved by simply passing well-framed ordinances or by distributing cuspidors. The people must be made aware both of the dangerous character of the disease and of the ease with which it may be combated. Only in this manner can we hope to bring about compliance with the regulations. The object in view is to be attained only by means of a comprehensive scheme of instruction.

The objection has been made that the public might become very much wrought up by an exposition of the dangers of the disease, and that the invalid, shunned and cast out of society, might lose the care due to his condition. Forebodings such as these are fanciful; they spring from the same source which has ever opposed the theory of the tubercle bacillus and all the other advances in bacteriology.

I myself and many of my colleagues have failed to find a single case in which instruction of this sort was the cause of disagreeable consequences to a patient, and yet we have been busied for the past eleven years in disseminating the doctrine of prophylaxis among the people. But even if overanxiety and untoward consequences did occasionally result, such isolated instances could hardly be considered in view of the great object to be attained, since in tuberculosis, as in cholera, leprosy, and other plagues, the welfare of the individual must be sacrificed to that of the community.

Finally, it is hard to discern the cause of this anxiety. Indeed, there was previously far better ground for it. It is certainly horrible to think, as is taught by those who accept the inheritability of the disease, that a man comes into the world burdened with the bacillus, and that he must sooner or later fall a prey to its ravages. The fear of contagion, also, must have been terrible at the time when danger was believed to lurk in every breath of the consumptive, and the least association with him was avoided. Nowadays, however, the terror of contagion is past. *We admit that there is danger in sputum, but, at the same time, teach a simple means for avoiding it. Prophylaxis is inspired by the idea that the consumptive, if scrupulously clean, is not a source of danger even to his immediate environment.*

This instruction must come from the physician. It must be carried into the daily papers, especially into those papers which are read by the common man, and into almanacs, magazines, and weeklies. It must work its way into the schools, and into the magazines of the young, and should actually be made a matter of daily routine, until the necessity of a careful disposition of sputum has passed into the very flesh and blood of the people. Much can be accomplished in this direction by the clergy, by the teachers in the higher and the lower schools, and by officers in the army and navy.

The necessary instructions could be imparted to the patients, their relations, and the nurses, especially to those patients dependent upon sick-funds and the inmates of institutions, by means of a brief set of printed rules, such as I have personally made use of for the last ten years.

My instructions have the following form:

Safeguards Against Consumption.

The most general disease of mankind is consumption (*tuberculosis*). *One-seventh of all people fall victims to it. In Germany alone almost* 130,000 *persons die of it annually.*

The disease originates through the inspiration of the germ of the disease, a so-called bacillus. It is infectious, i. e., *one man gets it from another. It is* not, *however, in* the expired air *or in the* exhalations from the invalid *that the danger lurks, as was once believed.* Infection *ordinarily occurs* through the sputum, *especially when this is voided by a consumptive upon the* floor *or into a* handkerchief, *where it* dries, *and, becoming* disseminated as dust, *is again* inhaled *by healthy individuals.*

Many other diseases, e. g., *diphtheria, inflammations of the lung, and various catarrhs, are transmitted in the same way.*

The drying of sputum is a source of danger, *not only to those who come into contact with consumptives, but also to the invalids* themselves, *inasmuch as they are apt to re-inhale the bacteria which they have expectorated and permitted to dry, and thus infect portions of the lung which were previously healthy.*

Such infections can be avoided if consumptives, and indeed all *persons, take the trouble to keep the* expectorated material from drying *up; if* instead of spitting *into a* handkerchief *or on the* floor, *they take pains to spit into some* vessel *which can be emptied into the closet.*

All places in which there may seem to be any need for it, but especially closed rooms frequented by men, should be provided with cuspidors. It is best not to fill these with sand or sawdust, but to keep them empty or containing only a little water. They should be liberally *distributed, not only in every room, but also placed in all workshops, offices, schools, public places, corridors, staircases, etc., in order that people may find it convenient to obey the regulations.*

If these conditions be preserved, association with consumptives, and the care of them is ordinarily without danger.

In factories, workshops, etc., spitting upon the floor or into handkerchiefs should be strictly prohibited by printed notices. Cleaning should be done moist, *with the window open.*

On the street, where spitting on the ground is almost unavoidable, the danger of infection is lessened by other conditions, i. e., *sunlight and moisture.*

Every one *should make it an* invariable rule *to* expectorate *into a* vessel, even in case of simple cough, *and* never *upon the* floor *or into* handkerchiefs.

As far as possible, only boiled milk should be used, especially if it is intended for children, or the sick or convalescent. In dusty or suspicious atmospheres one should always breathe through the nose.

The consumptive, when he abides by these rules, is hardly to be considered as a source of danger to his environment. Moreover, since the bacilli are not able to live for more than half a year or so outside of the body, we may expect that the regulations will lead to a pronounced diminution *in the* disease. *As a* matter of fact, *the* disease *has become* less prevalent *in Prussia since individuals have become more careful with their sputum. For, whereas in* 1888 *and in all the previous years, about* 84,000 *persons annually died of tuberculosis, there has been a steady decrease in the number since that time, in spite of an increase in the population, so that in* 1896 *only* 70,000, *in round numbers, succumbed to the disease; in other words,* 14,000 *less than before.*

A few years ago a similar course of instruction was undertaken by the New York City Board of Health, coupled with the demand that physicians should report all cases of tuberculosis. There was great opposition at first to the latter regulation, but year by year the physicians complied more willingly and in greater numbers with the demands of public health.

It is well to put up notices with the categorical imperative: "Do Not Spit on the Floor," in all public buildings, saloons, schools, offices, waiting-rooms, restaurants, boarding-houses, staircases, horse-cars, and steam-cars, and in all public conveyances, and these notices should be put up near the cuspidors.

Of the 800 consumptives whose histories I took, a not inconsiderable proportion was aware of the danger from sputum, having learned it for the most part not from physicians but from the newspapers.

We cannot, of course, expect to uproot at once old customs and bad habits, but we should not underestimate the force of a suggestion which is repeated over and over again, particularly where there is no question of self-denial, as in alcoholism, or of a means of personal decoration, as the corset. The people must be educated to cleanliness. They must be taught to regard expectoration on the floor as no less indecent than the satisfaction of the demands of nature *coram publico,* a habit which was once considered hardly objectionable. Indeed, the erection of public closets is a matter of very recent date.

[In a number of cities in the United States ordinances have been passed, and are being enforced, making expectorating upon the floors of public places and vehicles a punishable offense. Within very few years the majority of the public have accepted the legislation, and show an interest in the enforcement; while in several cities, New York, for example, there is in consequence a noticeable improvement in the cleanliness of such localities, and the coincident improvement in the tuberculosis statistics may fairly be ascribed in part to this change.—Ed.]

GOVERNMENTAL REGULATIONS AGAINST ANIMAL TUBERCULOSIS.

The coöperation of the state is absolutely indispensable in the campaign against animal tuberculosis. It should certainly eradicate tuberculosis from cattle by gradually removing all the infected animals. The recognition of the diseased animals is possible through the use of tuberculin.

Two objections have been raised to the use of tuberculin: in the first place, that it is uncertain, since tuberculous animals may fail to react and vice versa; and in the second place, that tuberculin often causes a rapid dissemination of the process.

According to a collection by Voges of the results of inoculation by seventy authors, the findings being subsequently verified at autopsy, 7327 cows inoculated with tuberculin gave the following results:

	Reacting Positively: 6840		Reacting Negatively: 487	
	Tuberculous.	Non-tuberculous.	Tuberculous	Non-tuberculous.
Of these at autopsy there were:	6684	156	48	439

that is, an error of 204, or 2.78 per cent.

The margin of error is certainly not great, and becomes even smaller if we allow for errors in autopsies and in experimentation. The absence of tuberculosis in certain of the animals which reacted, as above shown, cannot be accepted without question, inasmuch as the examination was restricted in some cases to the simple inspection of individual organs, so that small foci or foci in other organs would have escaped detection. The 48 animals, or 0.65 per cent., which failed to react in spite of the existence of tuberculosis, do not essentially modify the result. Some of them were given doses which were too small; others were the victims of a generalized tuberculosis, and were thus immune, although easily to be diagnosed in other ways; still others possessed calcareous, *i. e.*, healed, foci, and would have reacted to a subsequent inoculation in case they contained living bacilli.

The assertion that the animals suffer through the injections has not withstood the test of experience, with the exception of a few cases of advanced tuberculosis, as has been shown by Bang in injections into 52,000 cattle.

The temperatures of the animal under investigation should first be accurately determined by daily measurements, best taken toward evening, for one or more days before, and then injections of tuberculin should be made, varying in strength according to the size of the animal—for calves 0.1, for cows 0.5, for heavy bulls 0.6 cc. Animals with fever should not be subjected to the test. The reaction, which usually occurs within twelve to twenty hours, may be measured after nine, twelve, fifteen, or eighteen hours. An increase of 1.5° C. above the normal, or a rise above 40° C., is evidence of tuberculosis, while a rise of less than 1.5° C. justifies a suspicion of the disease.

Observation has revealed that a subsequent inoculation, even months later, may give a doubtful reaction or even none at all, in spite of the fact that the animal has not recovered from the disease. In this regard animals differ from the human species. Dishonest dealers make use of this fact, by giving an animal which they wish to sell an earlier injection of the tuberculin, thus rendering it immune to the dose which is a necessary preliminary to the sale.

For this reason:

(*a*) the sale of tuberculin should lie within the control of the government, and should be made only to veterinarians for the express purpose of making injections for diagnosis and with a guarantee against fraudulent use. The price of tuberculin should be made exceedingly low, in order to facilitate its more general use for purposes of diagnosis.*

(*b*) The inoculation is always to be performed by an experienced veterinarian.

(*c*) The animals so tested, both those which react and those which do not, should be marked in a manner denoting the date and the result of inoculation.

Denmark, especially, has set the pace in the diagnostic inoculation of tuberculin for the purpose of exterminating the disease in cattle.

All animals found to be tuberculous should be separated as far as possible from the others, in order to prevent the spread of infection. Early slaughter would be the safest means, and would also serve the best interests of the owner, since the animal both assimilates less food and gives less milk as the disease progresses, and thus continually loses in value. Practically, however, it is necessary to restrict this measure. The disease has become so widely disseminated, involving as many as 50 or 70 per cent. or even more of some herds, that the sudden swamping of the market with meat would result in a considerable fall in price and a corresponding loss in property to the owner. Chief stress, therefore, should be laid on the separation of the diseased cattle from their offspring.

There should be a partial remuneration, by means of mutual—perhaps compulsory—insurance, for the pecuniary loss incident to the possession of tuberculous cattle, and there should also be premiums upon the possession of healthy herds.

In order to obviate the dangers from tuberculous meat (see page 139 et seq.) there should be a general inspection of all meat offered for sale, and diseased specimens should be rejected.

(*a*) All meat should be rejected as dangerous to health and useful only for manufacturing purposes, if the meat itself appear diseased, or if the bones contain pearly nodules, or if the disease is general and severe, *i. e.*, involves more than one of the body cavities and is associated with much emaciation.

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* In Hesse, for example, the government sells a half a gram of tuberculin for 35 pfennigs [about 8½ cents].

Such meat should not be used either fresh or cooked, or eaten by either men or animals.

(*b*) If the disease involves two of the body cavities, but without necessitating the assumption of a dissemination by means of the greater circulation, if, moreover, there is no emaciation and the meat appears to be sound, it may be designated as of inferior quality but not dangerous to health.

Such meat is to be sold only after having been cooked.

The cooking is done in a steam-chamber; the pieces must not weigh more than five kg. and must be kept for half an hour at a temperature of 100° C. (The same regulation holds good in Saxony.)

(*c*) If the tuberculosis is confined to only one of the body cavities, or to a single organ, so that dissemination by the greater circulation may be excluded, the meat is to be considered neither detrimental to health nor of inferior quality.

Such meat may be freely offered for sale, after elimination of the diseased portions.

Many countries have regulations which approximate the requirements above detailed.

The milk, butter, and whey establishments should also be subject to supervision, with reference to the cows from which the milk is obtained.

Here, too, the individual can protect himself from infection, either by getting his milk and the milk products entirely from establishments under official supervision, or by boiling the milk sufficiently before using it.

Every farmer and cattle-owner can contribute largely to the improvement of conditions within the narrow sphere of his own possessions by acting in the spirit of the preceding rules. He should isolate those cattle which the injection of tuberculin has shown to be diseased, inasmuch as their cough and their infected nasal mucus render them dangerous both to man and beast. He should keep tuberculous men and girls from tending the cattle or assisting at the milking, or should at least insist upon the observation of precautionary measures. He should exclude tuberculous individuals from the stables, *i. e.*, should not offer milk to drink in the stable.

Our demands are simple, at least in so far as concerns the avoidance of tuberculosis among men. They differ from the earlier suggestions, which were made before and shortly after the discovery of the tubercle bacillus, in that they are not based upon all sorts of purely theoretical notions, and do not demand the disinfection of each particle of sputum, the isolation of patients, prohibition of marriage for consumptives, separation of parents and children, and other impossibilities.

The simpler the regulations and the more precise the demands, the more likely are they to meet with compliance. Having found, therefore, that the moist disposal of the sputum is of chief importance, we avoid providing for every possible contingency in the way of infection. It would only produce practical difficulties, confusion, and disturbance, and would obscure the main issue, if we attempted to pay regard to such minutiæ as might possibly tend to produce infection, *e. g.*, chewing on penholders, explosive coughs, flea-bites, contamination of food by infectious dust, etc.

If one takes a larger view, and grasps the root of the evil, the rare and occasional modes of infection may be disregarded.

The emphasis which is laid upon predisposing circumstances is of no value for purposes of popular instruction, great as may be their actual importance. Individuals rarely have it in their power to influence these conditions. Of what use is it to the great masses, if one preaches that they should live and work in large, airy apartments, should eat well, and should exercise freely in the open air, when stern necessity and the earning of their daily bread compel them to labor in dust-laden atmospheres? Why should the individual be careful with his sputum, if he is continually told that other matters, which he has no power to alter, are of more importance? There is no doubt that the emphasis laid upon predisposing conditions has largely interfered with the success of prophylactic measures in many countries.

RESULTS OF PROPHYLAXIS.

I have at times been met with the objection that the execution of these prophylactic measures was impossible and visionary, and I have been confronted with the failure of previous attempts, as in Naples and in Portugal.

In Naples, toward the end of the last century, a decree was passed which made it obligatory for physicians, upon pain of a penalty of 300 ducats or of ten years' banishment for repeated offenses, to report every case of pulmonary consumption (ulcera pulmonalia), which, in addition, gave to poor consumptives the privilege of admission to the hospitals, and required burning of all suspected furniture.

This decree—which, by the way, is a tribute to the infectious character of phthisis long in advance of the discovery of the bacillus—naturally touched only the very sick, whereas the vast majority of the chronic ambulatory consumptives, who constituted the chief danger, were not affected by it, so that, *à priori,* no very great benefit could have been expected to accrue.

There is no longer room for dispute concerning the success of the prophylactic measures which I previously advocated. The discovery of the tubercle bacillus had already made men more careful. After I had succeeded in overthrowing the hypothesis of ubiquity and thus putting prophylaxis upon a firm basis, my suggestions became the point of departure of numerous regulations, at first in Prussia and in the narrow confines of asylums, prisons, and hospitals.

The first regulation emanated from the Berlin police. The second, based upon a recommendation of the Royal Prussian Scientific Committee for Medical Matters, was coupled with an attempt to secure its dissemination among the people and the press. In addition, a series of attempts were made by the various governmental ministries, by the physicians of the general staff and by the provincial staff, which cannot here be described in detail. Subsequently the governments of various other countries followed suit, although with less energy.

Moreover, the question of prophylaxis was ventilated in many popular writings and lectures; I need only refer to the labors of Predöhl in Hamburg, of P. Dettweiler, Günther, Meinert, Heller, G. Merkel, Rochelt, Felix, Flick, Tyndall, and many others. It became the subject of discussion in many medical societies. Even the political press engaged in the discussion, and thus insured the popularization of the regulations.

These measures were rewarded by a considerable decrease in tuberculosis. The mortality from the disease fell in the following manner, reckoned on a basis of 10,000 of the living. In the Prussian:

Prisons........	from **118**	in the years 1875–1878	to	**81**	in 1892–94.
Asylums.......	from **184**	in the year 1888	to	**156**	in 1891.
Nursing societies	from **100.4**	in the years 1887–1888	to	**67**	in 1893–94.

The favorable effect of the prophylactic measures in these institutions is therefore undeniable. The mortality from tuberculosis was lower by several hundred persons than might have been expected from the average of previous years. Since, however, the numbers are rather small for statistical conclusions,—about 11,000 in the prisons, about 35,000 in the asylums, and 3000 living persons in the nursing societies each year,—there is a possibility, though not a strong probability, of error.

But even if the mortality of the entire state is considered, a notable diminution can be made out, especially in Prussia, which took the initiative, at the instigation of the minister von Gossler, in deducing practical conclusions from the teachings of science, and in leading the way toward a prophylactic treatment of tuberculosis. In the other states of Germany and in Austria, in which the government took up the cause of prophylaxis later or not at all, leaving it to the people to teach and protect themselves, we find that the decrease in the mortality from tuberculosis is far less marked. (See tables and diagram.)

Year.	To Every 10,000 of the Living, there Died of:							
	Tuberculosis.		Pulmonary Consumption.			Consumption.	Pulmonary Consumption.	
	Prussia.	Bavaria.	Saxony.	Baden.	Hesse.	Hamburg.	Alsace-Lorraine.	Austria.
1876	31.0	—	23.6	31.6	—	31.2	—	—
1877	32.0	—	25.0	30.4	28.5	33.0	—	—
1878	32.5	—	26.0	29.4	27.2	33.7	—	—
1879	32.5	—	25.8	31.5	27.6	33.5	—	—
1880	31.1	—	25.8	28.3	26.9	31.5	—	—
1881	30.9	—	23.8	28.6	26.1	31.5	—	38.5
1882	30.9	—	23.6	30.7	27.1	30.9	—	38.1
1883	31.8	—	24.6	31.2	28.2	33.1	—	40.4
1884	31.0	—	25.1	29.9	26.3	34.7	—	39.4
1885	30.8	—	25.0	32.2	29.2	32.6	—	40.7
1886	31.1	—	24.9	30.5	29.2	30.8	30.4	40.1
1887	29.3	—	23.0	27.8	27.0	30.9	28.8	37.2
1888	28.9	33.4	23.5	29.6	29.0	30.9	30.9	38.6
1889	28.0	31.5	23.8	27.7	28.3	26.8	28.7	36.2
1890	28.1	33.5	24.2	29.2	30.1	26.2	28.9	39.7
1891	26.7	32.9	21.6	27.1	27.1	26.5	27.9	36.6
1892	25.0	31.3	20.8	26.0	24.1	25.3	25.4	36.9
1893	25.0	31.5	21.5	27.1	27.0	24.0	24.8	35.4
1894	23.9	31.6	21.4	28.2	26.0	20.8	25.7	37.3
1895	23.3	31.1	21.0	26.7	25.8	21.0	23.4	—
1896	22.1	29.4	20.1	26.5	24.3	20.4	22.3	—
1897	21.8	30.0	19.8	25.5	—	20.1	—	—

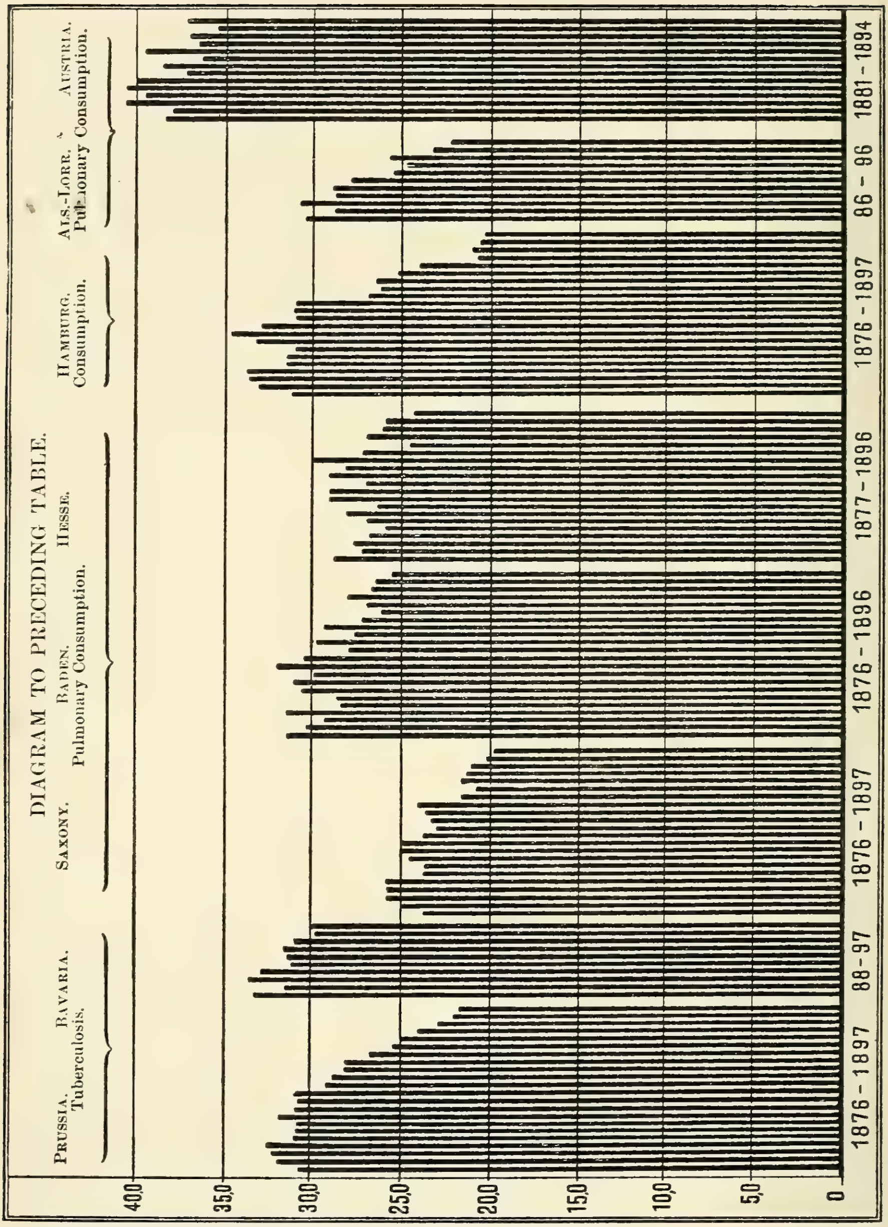

DIAGRAM TO PRECEDING TABLE.

The decrease in tuberculosis, which persists in spite of an intervening epidemic of influenza, is too great to be due to chance causes. Neither does it depend upon a shifting of the causes of death, but goes hand in hand with a lowering of the total mortality, so that the decrease represents an actual gain in human life. Indeed, the decrease of tuberculosis tends indirectly to lower the figure from other causes, in part by lessening the mortality from diphtheria, in part by improving general conditions.

The decrease in the mortality from tuberculosis, which I determined in 1894, has been confirmed recently for the imperial health commission by Rahts.

Never before, as far as figures show, did the mortality from tuberculosis fall so low as it is to-day. Formerly, it oscillated between 32.5 and 30.8 per 10,000 of the living; the tendency toward a decrease, due to a certain degree of caution which followed upon Villemin's researches, and especially upon Koch's discovery of the tubercle bacillus, was but slight. From the year 1889, however, there has been an almost *steady decrease* from the previous average of 31.4 to 21.8 per thousand, *so that* in the period of 1889–1897 the mortality from tuberculosis was *about* 184,000 *persons less than was to have been expected according to the average of* 31.4 *in previous years.* The gain to human life is about four times as great as that which has as yet accrued from the use of Behring's antitoxin, the latter having reduced the mortality from diphtheria by about 50,000. *The frequency of tuberculosis has fallen, therefore, to about two-thirds of what it previously was.* And yet the scope of prophylaxis has hitherto been very limited.

In other states also there has been a diminution in the frequency of the disease, although, for reasons already stated, this has not been so pronounced as in Prussia.

In Saxony the mortality from tuberculosis has been lessened by 7700, in round numbers, since 1890; in Hamburg, by 4000—figures which are to be taken in comparison with the smaller size of the population.

The resistless force of these figures, at once a proof of the necessity for, and a justification of the thousands of experiments upon animals, which alone could serve to teach us the conditions underlying infection, are sufficient to refute all the theoretical objections which were at one time urged against my prophylactic measures. They also demonstrate the correctness of the premises, the practicability and the success of the antibacillary prophylaxis of the past, and make it incumbent both upon the individual and the state to institute further measures.

INDIVIDUAL PROPHYLAXIS.

Although strong persons often succumb in a very short time to a tuberculous infection, nevertheless it holds as a rule that the disease is more difficult to control or cure, and proves more rapidly fatal, among weaker individuals. Our efforts must, therefore, be directed toward strengthening the organism in every way. The means toward this end comprise all hygienic measures. I shall, however, point out the chief indications.

In case of weak children, watchful care should begin in infancy. As a matter of course, they should not be nourished by a sick mother. They should be fed only with milk which has been sterilized (Soxhlet's apparatus), unless its source is absolutely unimpeachable. The health of the wet-nurse, of the nurse, of the governess, of the attendants in general, should be assured. If any member of the family (taken in the broader sense) is tuberculous, such a one should be kept as far as possible from close association with the child, should be forbidden to kiss it, and admonished to be careful in the dispcsal of his sputum.

In the nursery, carpets and other lodging-places for dust should be banished. The nursery should be kept as clean as possible, but especially the floor, on account of the danger from bacilli brought in on people's shoes. The danger is enhanced by the fact that children have the habit of playing about on the floor and then sticking their fingers into their mouths. These paths of infection are to be kept closed as far as possible, by keeping the hands and the body clean. Cleanliness, indeed, should be the key-note of the nursing and education of the child from the cradle up.

As far as is permitted by school work and other conditions, as much time as possible should be left free for recreation in the open air. This means nothing else than cleanliness of the lungs, for we know that the open air is far purer than that of rooms.

When the child goes to school, the health of his schoolmates and their relatives is also a matter for consideration. How often it happens that a child whose parents are scrupulously careful goes to visit a comrade in whose family there is a consumptive: At play a good deal of dust is generally raised, and the child brings home the germ of tuberculosis as well as of other diseases. Under such circumstances it is a piece of folly to trace the germ back to some long dead grandmother.

Children should be brought up not to be capricious about their diet, but to eat heartily of coarse and healthful food. The foolish notion of young girls to eat little and to select acid foods, in order to remain slim, should be frowned down. Chlorosis should be combated by a timely course of iron, air, and water. Above all, attention should be paid to any diseases, especially such as interfere with nasal breathing, *e. g.*, adenoids, etc., inasmuch as mouth-breathers are much more subject to infection. Brine baths, especially in the mountains, and sea baths are calculated to strengthen the general constitution.

The practice of giving alcohol and "strong wines," especially in large doses, to weakly children, cannot be sufficiently condemned.

The choice of an occupation should be in favor of such as do not entail the inhalation of dust and close confinement.

Individual prophylaxis consists in part also in the avoidance of infection, for, after all, the *punctum saliens* in breathing is to obtain sterile air. The invigoration of the body and of all its parts, including the ciliated cells, affords a means of eliminating the bacilli. It is not known how this is accomplished—whether the tissue juices are altered so that they afford less nourishment to the bacteria, or the cells are more resistant, or that encapsulation is more rapid on account of an increase in the irritability of the tissues or a decrease in the absorption of the proteins.

Good, hearty food, plenty of fresh air, care of the skin, and exercise, these are the means of protection against the infection and, to a certain extent, against the disease, which are at the disposal of the weak in every stage of life. Therefore, these measures should characterize the treatment of the early period of phthisis.

A number of other recommendations are undoubtedly very important and valuable—a healthy, dry, and sunny house, avoidance of narrow and crowded streets, moderate mental and physical exertion, avoidance of excitement, of multiple childbirths—but they are generally overborne by the fierce realities of life, by social requirements, by the struggle for bread, by love and sorrow.

CHAPTER VIII.

THERAPY.

The therapy of pulmonary phthisis is general (hygienic and dietetic), specific, and symptomatic.

HYGIENIC AND DIETETIC TREATMENT.

Specific therapy should logically form the basis of treatment, but it has as yet shown no results which would entitle it to this position. At present, hygiene and diet are the chief factors in the treatment. We cannot enter into the description of this method without recording our gratitude to the man who did so much to establish it.

It was Brehmer who from his little mountain hamlet of Görbersdorf proclaimed *urbi et orbi* at the close of the fifties that phthisis was curable, not alone spontaneously, but also by means of energetic and skilful treatment. Many of his premises were false, but, fortunately for mankind, he stuck to his belief, unmoved by enmity, sarcasm, or contradiction. His cures grew in numbers and reputation, and through them physicians came to regard the consumptive as a hopeful case, instead of one predestined to perish.

Dettweiler, a pupil of Brehmer's, gave especial attention to the innumerable variations in the course of phthisis, and labored to perfect this mode of treatment.

Our present-day treatment of phthisis is, essentially, nothing more than a heightened hygiene of the body and mind. We have to deal with an individual in imminent peril of death. Every means must be invoked to maintain the life processes at the normal or to bring them back into physiological condition if diseased; the losses which the body has suffered must be repaired; and the most insignificant set-back, which in health might be overlooked, but which might on his perilous journey precipitate the consumptive into the abyss, is sedulously to be avoided.

No single element in the cure, neither air, nor food, nor hydrotherapy, nor medicine, affords any guarantee of success; it is only the satisfaction of all the physiological and hygienic demands of the organism, from the *greatest to the least significant, that can bring about this result, and of this fact the physician should not for a moment lose sight.*

Phthisis, even in the early stages, is a severe disease, and we can hardly expect that there will be an improvement within a few days or even weeks.

Success comes only to him who devotes himself to his task with unwearied patience, to him who strives with iron determination toward the goal, undaunted by the relapses which so frequently occur. In hardly any other disease is the personality of the physician, outside of his science and his art, of such importance as in phthisis; indeed, the psychical management of the patients is a cardinal factor in the treatment.

PSYCHICAL TREATMENT.

The physician who merely gives the necessary directions concerning food, rest, and medicine, even though these be elaborated with the utmost care and skill, can never have the same success as one who takes the trouble to establish a bond of sympathy between himself and the invalid. This fact depends in part upon the prolonged course of the disease, in part directly upon the psychical changes in consumption. The patient has no energy, weakens easily, and needs a strong support, which he seeks to find in the physician; to the physician he must abandon himself with complete confidence. The physician must earn this confidence by the clearness and the definiteness of his directions, and by his inflexible perseverance in the course which he judges best for the poor unfortunate battling for life. He must study the mental condition in order to discover the proper way to influence him (Heinzelmann). Frivolity must be met with sternness, ignorance by benevolent instruction, and foolish conduct by firmness and constancy. The emotional must be strengthened, the hypochondriac stimulated. The right word in the right place often does more good than the best medicine.

The physician alone can accomplish nothing if the patient does not coöperate. The will-power and the endurance of the latter are subjected to an extraordinary test, which he will hardly be able to withstand unless he realizes that his life is at stake. In common with Brehmer and most other physicians who have had much to do with consumptives, I hold it proper to *explain the nature of his disease* to the patient. Deception, even to-day largely in vogue, should be discarded; such euphemisms as "apical catarrh" and "pulmonary catarrh" are responsible for many a life.

A man with a simple apical catarrh, otherwise strong and healthy, has no inducement to take special care of himself. How can he be brought to observe the innumerable precautionary measures, to renounce his favorite habits and pleasures for years? How can we justify our demand that he temporarily abandon his vocation, that he leave his home and family, and freely sacrifice his time and money, if we conceal the seriousness of his affection?

Formerly the diagnosis was tantamount to a sentence of death, and it would have been inhumane to publish it. To-day, however, our diagnosis goes hand in hand with the information that the patient is suffering from a severe disease, of which he will die unless he takes care of himself, but with the confident assurance that he, like so many before him, will in all human likelihood get well again, if he rigidly follows our instructions. Talk of this kind is no longer brutality, but actually necessary, in order to bring about the untiring coöperation of patient and physician. How often have I heard this complaint from some consumptive: "If I had only known what was the matter with me, I should have taken better care of myself, but I was told only of an apex-catarrh." Is not this a heavy accusation against the first adviser?

The patient is naturally shocked to learn of the severity of his ailment, but I have never found that the accompanying proviso failed to give him courage. Thanks to the hopefulness which a wise Providence has implanted in the human breast, he again braces himself, and hope and fear make him resolute to do everything that his deliverer deems necessary.

The truth cannot always be exposed at once; tact and sympathy must guide the physician. When the anxious look, the trembling tongue, betray the intense agitation of the sufferer, he will only gradually and cautiously impart the diagnosis to his patient. We must, however, insist that truthfulness increases trust in the physician, and greatly lightens his task. In the advanced stages the patient has generally made the diagnosis himself. In hopeless cases the information is to be given only in order to protect others from infection.

Once we have explained the nature of the disease to the patient, we should admonish him to be careful with his sputum, and should warn him, above all, not to swallow it.

NOURISHMENT.

The most noticeable effect of consumption is the progressive emaciation. Our first aim must be to stay the increased metabolism, to make good the pressing deficit, and by a heightened nutrition to cover the loss which has already occurred. If my theory is correct that the rapid waste of the tissues tends to hasten absorption of the proteins surrounding the tuberculous foci, and thus at the same time inhibits the natural process of healing by means of induration, and also furthers the peripheral distribution of the bacilli, forced feeding is not only a symptomatic measure, but directly furthers the cure. It furnishes no protection, of course, against dissemination by aspiration. Further, a good state of nutrition improves the blood, the strength, and the resistance of the cells.

All dietary rules for the consumptive must be detailed, clear, and exact. It is folly to expect results from such orders (unfortunately not uncommon) as: "Eat well, drink a good deal of milk, and take walks." The patient knows as much as before. We must prescribe the exact time of eating, and, as far as possible, the quality and quantity of his food. The dietary which I have prescribed, with variations, for my well-to-do patients for the last eleven years is somewhat as follows:

First breakfast, 7.00 to 7.30: One-fourth to one-half liter (quart) milk (cocoa, coffee) with one or two eggs stirred in, or gruel, or meat, bacon, bread and butter.

Second breakfast, 9.00 to 9.30: One-fourth to one-half liter (quart) milk, or 100 cc. (3 ounces) strong wine (sherry, port, malaga, marsala), bread and butter.

Meal preceded by one-fourth to one-half hour of rest.

Noon meal, one o'clock: Soup, entrée, fish, roast, venison, fowl with vegetables, preserves and salad, pudding, butter and cheese, 100 cc. (3 ounces) red wine or one-fourth liter (one-half pint) beer.

Meal followed by one-half to one hour of rest, perhaps of sleep.

Afternoon meal, four o'clock: One-fourth to one-half liter (quart) of milk (cocoa) with one to two eggs stirred in, bread and butter (honey).

Supper preceded by one-fourth to one-half hour of rest.

Supper, seven o'clock: Roast meat, vegetables, cold meat (ham), roasted potatoes, bread and butter, 100 cc. of wine or one-fourth to one-half liter (quart) of beer, milk.

Nine o'clock: One-fourth to one-half liter (quart) of milk, one zwieback, cakes or bread.

The rest before meals, which I prescribe even for fairly strong patients, increases the consumption of food.

In order to control the results of our dietary, we should always keep track of the patient's weight. Unfortunately we cannot estimate the proper weight for the invalid, since this varies with age, size, and sex, and there are no weight tables constructed upon a sufficiently broad basis.

It is best to weigh the patient once a week, at the same time, the same day of the week, preferably before stool and breakfast, with the same clothes, and upon a good scale (not automatic). The weights should be entered in a book. Allowance should be made for increase of weight due to edema. The scale serves, to a certain extent, as a control both for physician and patient, and indicates the diet.

It is well to take daily note of the food consumed, both quantity and weight. This keeps us well informed, and at the same time accustoms the patient to method and to self-observation. For this purpose, von Leyden and Jacob have made up very satisfactory tables of nutrition.

A healthy adult needs about 120 gm. of albumin, 50 gm. of fat, and 500 gm. of carbohydrates daily. The various articles of diet may be approximately represented by their combustion values, and it is therefore advisable to estimate the value of the food in calories. Since albumin yields 4.1 units of heat, fat 9.3, and carbohydrate 4.1, it is only necessary to multiply the number of grams of albumin in the food by the corresponding figure, and likewise with the other constituents, and then add the products. The daily diet, therefore, yields:

Albumin	120 by 4.1, or	492 calories.
Fat	50 by 9.3, or	465 "
Carbohydrates	500 by 4.1, or	2050 "

An individual at rest consumes about 30 to 35 calories per kilo of body-weight a day, while one doing light labor uses about 40. An adult of average size consumes about 3000 calories, and his food should contain this amount of combustible material. A consumptive uses still more, yet occasionally an emaciated individual gains weight under a diet of 24 to 27 calories per kilo (von Noorden).

In order to give an idea of the value in calories of the various articles of diet, I append a table of the equivalents of the most common foods in a quantity of 100 gm. (0.1 liter), according to calculations made by Boas and myself. It is difficult to give figures of practical value, because, in the first place, the raw stuffs vary in composition, and, secondly, because the nutritive values are largely altered in the preparation and much increased by the liberal addition of butter and sugar. The assimilability of the foods is also a factor in the net result.

There are in:

100 Gm. or 0.1 Liter.	Calories.
Milk	67
Skimmed milk	40
Cream	215
Buttermilk	41
Butter	756–807
Pot-cheese	179
Swiss cheese	340
Scrambled egg	188
One egg	70–80
Beef, raw	119
Beef, boiled	209
Beef, fried	214
Veal cutlet, raw	142
“ “ fried	230
Calves' brain, raw	140
Sweetbreads	90
Pork, fat	313
Bacon	617–761
Chicken (breast), raw	100
Tongue	393
Smoked meat	255
Smoked ham	438
Pommeranian goose's breast	381
Bologna sausage	445
Liver sausage	290
Carp, raw	93
Pike, raw	72
Turbot, raw	101
Trout, raw	106
Salmon, raw	133
Haddock, raw	61
Sole, raw	95
Perch, raw	76
Oysters, raw	20
Pickled herring	246
Smoked salmon	224
Kiel sprats	243
Caviar	278
Rice cooked in milk	177
Mashed potatoes with butter	127
Spinach, raw	39
Spinach, boiled	166
Carrots	41
Purée of beans	193
Peas	75
Beans	41
Asparagus	18
Farina pudding	288
Omelette soufflé	237
Noodles (macaroni)	353
Raw sugar	406
Corn bread	203–232
Pumpernickel	229
Wheat bread	229–260
Zwieback	332–358
Cakes	374
Corn brandy	280

The indication is easily fulfilled in invalids with healthy digestive organs. Without excluding this or that, the dietary gives the patient a fairly wide choice, and demands only that he select a fairly mixed diet in sufficient quantities. Concerning the value of the various foods, I refer to the excellent articles in the "Handbook of Dietetic Treatment" of von Leyden, as far as they have yet appeared.

An exclusive meat and egg diet, which is often forced upon the invalid by his family, does not fulfil the purpose. The preference for the so-called white meat is not justifiable: in addition, one should give fat, fowl, goose, duck, pork, mutton, veal and wild boar—the latter also in brine. If the fatty tissues are deficient, fats should be given in every form which the patient can stand, from butter and cream, which are easily digested, to the less digestible hog and goose fat, in so far as they do not provoke cough.

The fatty fish, also eels, salmon, sardines and sprats, should often be on the bill of fare. In order to supply the demand for fats, every dish, even the vegetables, must be prepared with a great deal of fat, especially if the patient does not like fat as such.

The vegetables, especially the albuminous legumes, are easily digested in the form of purées, and are especially valuable because they make the meat more palatable. For the same reason, all forms of compote, salads and horseradish are to be recommended. As a rule, there should be a plentiful supply of vegetables with the first meat meal, and, in addition, if the means permit, compote, fruit marmalade, and oily, non-acid salads.

Carbohydrates, also, which increase the deposition of fats, are to be taken in sufficient quantities: puddings, pastry of all kinds, pies, food baked in fat, cakes, zwieback, honey, then the various kinds of bread, brown-bread, whole wheat bread, especially with constipation, graham bread, pumpernickel, also bread and honey.

An important feature is tasty and piquant preparation, with different spices and flavors, which encourage the appetite and stimulate the flow of gastric juice. Of these we have a liberal assortment to choose from,—vinegar, lemon juice, mustard, etc.,—to be used in just sufficient quantities. Variety is the great secret. Nothing is more likely to discourage the appetite of the patient than to know the menu days in advance.

All these matters demand individualization and not the fixed routine of a big hotel. It is of great importance that the meals should be taken exactly, I had almost said pedantically, at the same time, in order that the stomach may get into the habit of taking in food. The number of meals should be at least five. If the patient's appetite is not good, he should never eat between meals, even if he has the desire. The serving should be agreeable and not too slow. Food tastes better in pleasant company and with agreeable intercourse. If we physicians take interest in these details, we shall often discover why one or the other patient makes no progress.

Not too much should be put before the patient. He should chew his food well and impregnate it with saliva, but should not eat too slowly. (See Mendelsohn's excellent article in v. Leyden.)

Delicacies, oysters, caviar, etc., are of course permitted, but should be the exception. A good, healthy, household fare should be the basis of the diet. A time may come when we will be happy if the appetite is still aroused by these delicacies.

Loss of Appetite.—All these rules hold chiefly for consumptives blessed with a healthy appetite and a good digestion. Unhappily, anorexia and disgust for food may give us a great deal of trouble. If we have convinced ourselves that this anorexia is purely nervous in character, and that the motor and chemical functions of the stomach are normal, if we know by means of two-hourly investigations for several days that no fever is at the bottom of it, we can generally gain our point by an unvarnished picture of the evil which will result to him, and by the use of the categorical imperative. For such a patient can eat if he will; all he lacks is the energy, and this the physician must supply. The latter should even take the trouble to visit the patient at noon, and have him eat dinner in his presence. If the patient only realizes that he actually can eat, a good deal has been accomplished.

Not only eating is necessary. Very often, but of course only in case of strong patients, an occasional day of fasting works beautifully, and serves to acquaint him with the sensation of hunger.

One should not expect too much at once of patients who from youth up have been light eaters (and of this class there are not a few, especially among the girls and women of the better classes), nor from patients who have suffered for some time from partial inanition. In such cases *festina lente* is the rule. If the patient is terrified from the start by a dietary which he perforce confesses to be beyond his powers of consumption, he loses both his courage and his confidence in the physician. The best way is to ascertain the customary amount of food taken by the patient, and to increase this gradually day by day. Thus the stomach has a chance to get accustomed to its extra labor. On the other hand, there should be a steady and inexorable enlargement of the diet. *Nulla dies sine linea.* The danger which lurks in delay should stimulate us to expedite the increase of nourishment.

If there is an aversion to the ordinary articles of diet, we should try ragout, hash, sweetbreads,—a favorite dish in southern Germany,—calves' brain, and scraped meat fried in butter; if there is an aversion to hot meat, we may try cold; then we have condiments, such as anchovy and caviar. Or, we may begin with meat chopped very fine just before the meal, and gradually made coarser, which is then fried, and taken in teaspoonful doses with vegetables or compote. Gelatinous preparations, meat jelly and wine cream, also serve a good purpose. Semi-solid foods are always taken more willingly than solid, which must be kept in the mouth longer and be carefully chewed. For the same reason powder of meat is preferred, and eggs rubbed up, *e. g.*, with spinach. Eggs with red wine or eggs with milk and vanilla are often of use.

Often the anorexia depends upon deficient care of the mouth. A coated tongue and a bad taste deprive the food of its flavor and carious teeth interfere with chewing. Mechanical cleansing of the tongue with a spatula, care and treatment of the teeth, and the regular use of mouth-washes (*e. g.*, potassium permanganate, of which a 0.5 per cent. solution is added drop by drop to water until the color turns red, tincture of myrrh, water of balm—Melissenwasser), are various means to combat these conditions.

Often wet compresses (Priessnitz) over the stomach work well, or local moderately cold douches, general rubbing, or other kinds of hydriatic treatment. Lavage of the stomach may be necessary. Weak faradic currents are often of service. Only recently I treated a patient who resisted all other measures but would willingly eat, and digest, a moderate-sized meal half an hour after faradization.

In the struggle against loss of appetite, the bitters and carminatives often prove valuable allies:

Tr. rhei vinos 25 to 30 gtt. t. i. d. one-half hour before meal-time, or Tr. chin. comp. in similar doses, or both of these with Tr. zingiberis āā 30 gtt. t. i. d.

With orexin muriate as previously recommended by Penzoldt I have had no success. Orexinum basicum and tannicum (0.3 gm. t. i. d. one-half hour before meals) seemed to work better.

Good service is often done by Immermann's condurango wine, or Tr. strychninæ 3.0 to 5.0, Extr. condurango fl. 30.0, 15 to 30 gtt. t. i. d. one-half an hour before meals; for subacidity, the chlorids. Now and then, one (N. B.—*One!*) glass of good champagne one-quarter hour before meals, or a small glass of carbonated water, are of service; or a glass of Vermouth (de Torino); or Elix. aurant. comp. Hoffmanii, 20 to 50 gtt. one-half hour before meals; or—

℞.	Extr. Absinthii	10.0
	Aq. Menth. Pip.	12.0
	Tr. aurant.	ad 100.0

M. Sig.—One dessertspoonful t. i. d.

(Augustin.)

Or—

℞. Tr. Aloes
Tr. Chinae .... āā 10.0
M. Sig.—Fifteen drops t. i. d.

Or—

℞. Lichenis island. 25.0
coque per semihoram cum
Aq. dest. q. s. ad
colaturam 500.0
Sig.—Use during the day

(Liebreich and Langgaardt.)

The three cardinal points in the treatment of anorexia are constant sojourn in the open air, as complete rest as possible, and change of climate, and these three are often sufficient by themselves to improve the appetite. We shall return to these points a number of times, in connection especially with Weir Mitchell's treatment, the treatment of pyrexia, and the health resorts.

Milk Diet.—Milk, by virtue of its happy combination of all the nutritional elements (albumin, fat, carbohydrates, salt, and water), and also on account of its easy digestibility, holds an important place in the dietary. Yet its value should not be exaggerated. In order to maintain the normal equilibrium of the body, an adult on an exclusive milk diet would have to take 5 or 6 liters (quarts) a day, an amount which hardly any one could drink without disgust.

I rarely prescribe more than one and one-half liters (quarts) a day, and prefer to make use of other nutritious foods. Only at special times, and upon an almost exclusive milk diet, as after hemorrhages (see below), is it well to go over three or four liters (quarts).

A forced milk diet, as so often prescribed for consumptives, does not appeal to me, as the ingestion of such large amounts of fluid is apt to cause atony of the stomach.

Moreover, such large amounts of fluid increase the work of the heart and disturb the hydrostatic equilibrium. Although the heart in health can easily compensate for this strain, every extra demand upon the poisoned and poorly nourished heart muscle of the consumptive is to be avoided. Indeed, death often occurs through heart failure. Especial care is indicated in cases where dyspnea and cardiac palpitation upon slight exertion (climbing stairs) denote a beginning insufficiency of the heart.

On the other hand, one might hope that an increased ingestion of fluids would serve to wash out the body and purify it of the poisons. But in tuberculosis the question arises whether the peripheral poison zones are not at the same time washed out (see page 440), and the curative reaction thus interfered with.

The milk must come from a healthy animal, and must be taken free from germs. The danger of a tuberculous origin and other kinds of germ growth is to be combated by pasteurization (Soxhlet). It is a matter of taste whether the milk should be taken hot or cold; perhaps in summer or in cases with a tendency to fever it is better cold, whereas in winter or with a tendency to chilliness it had best be given hot. Digestive disturbances with a milk diet are often traceable to poor quality (change being then the remedy!) or to some mistake in the administration. A weak stomach bears milk better if taken in small amounts, a few swallows at a time, and in combination with brown bread, toast, zwieback, etc. If milk is drunk rapidly, an indigestible curd forms in the stomach. In case of an almost exclusive milk diet, it is best to follow Brehmer's advice, and to take one-sixteenth of a liter (quart) every quarter of an hour, *i. e.*, three or four liters (quarts) a day. If the patient is overhasty, he should get the milk by teaspoonfuls.

Many individuals have a real or fancied idiosyncrasy against milk, and do not stand it even if cautiously administered. In such cases it is often of value to add small quantities of coffee, tea, acorn cocoa, lime-water (one teaspoonful to a glass), salt, a pinch of borax, or, if necessary, a few drops of rum, cognac, cherry cider, or corn brandy, which should be well stirred in. The alcoholic ingredients should be sparingly used. If the patient becomes tired of milk, it is best to discontinue for one or two weeks and use some substitute for it, beginning again, however, as soon as possible.

If there is diarrhea, it is better to add lime-water, acorn cocoa, or goats' milk; if there is constipation, cream or seltzer water is indicated.

Good service is done by Gärtner's fat-milk, from which a portion of the indigestible casein has been abstracted by centrifuging, and which has thereby become richer in fats.

I would especially recommend cream, which has about three times the caloric value of milk, and may be ordered pure or added to milk. Patients like cream with pulverized pumpernickel.

In order to forestall a disinclination for milk, or in case this is already present, or if there is constipation, it is a good plan to alternate natural milk with sour milk, or with kefir or kumyss, which latter are also euphemistically known as milk champagne, because a part of the grape-sugar has been turned into alcohol and carbohydrates by certain bacteria. The other advantages of these preparations are a pleasant, piquant taste, and a slightly diuretic action.

Sour milk is made by letting the milk stand in a place protected from dust for one to four days. It may be taken with brown bread (also sugar).

Kefir is prepared according to a method discovered in the Caucasus, by adding the kefir ferment to milk. The ferment requires great care in preparation, and should not be watery, but thick, like cream. Varying with the length of the period of fermentation, one distinguishes a one-, two-, and three-day kefir. Alcohol is present to about 2 per cent. It is usual to begin with two-day kefir; in case of constipation, we use the one-day. It is at times advantageous to add a little sugar. The daily quantity should be one liter (two small bottles).

Kumyss, too, is fermented milk (generally of mares), which is much used by certain Russian nomad tribes, especially the Kirghiz and the Baschkirs. As much as sixteen bottles a day have been prescribed, but two to four small bottles in combination with other food ought to be sufficient.

Butter is the most digestible form of fat, and should be offered to the consumptive in every shape, especially sauces, and in large quantities.

Prepared Foods.—If the patient can stand the natural foods, these will of course form the basis of the dietary treatment. But if they are not taken in sufficient quantities, and do not suffice to cover the deficit, and also to provide a certain reserve for intercurrent losses, then the artificial foods are to be called upon, and generally serve to fill the breach. G. Klemperer is certainly right in condemning the indiscriminate use of these substitutes.

Meat and Albumin Preparations.—*Meat extract,* which is a paste-like extract of the constituents soluble in water, is of value, less by virtue of its nutrient matter, which is only small in amount, than as a spice to the food, as an appetizer, thanks to its pleasant odor and its richness in extractives. It is of use also on account of its stimulating action on the nervous system and its richness in certain materials necessary in constructive metabolism. It is best to give five to ten gm. (about two gm. of albumin) per diem, with soup, vegetables, or bread. In larger doses it excites the nerves, and through its richness in potassium salts depresses the heart.

Beef-tea likewise, is rather an appetizer of only slight nutritive value. One-half pound of lean meat, with salt but no water, is cut into fine slices and packed into a bottle, which is kept, tightly closed, in a water-bath at a temperature of 50° for two hours, and is then put into boiling water for one-half an hour. It is valuable, especially in febrile weakness. A half cupful is taken at a time, and, in case of vomiting, is cooled in ice.

Of the same character, are *Valentine's meat juice* (6.7 per cent. albumoses and peptone), and Brand's Essence of Beef, which are chiefly remarkable for their price, and are therefore best replaced by Puro (made by Dr. Scholl in Thalkirchen), which is not only much cheaper, but is willingly taken by the patients. It contains about 2 gm. of extractives and 3 gm. of albumin in every 10 gm.

Of real nutritive value, and capable of increasing the body-proteids even in the absence of a sufficient secretion of hydrochloric acid, is *meat powder* (about 85 per cent. albumin).

Meat is cut into small pieces, dried in a water-bath, or roasted upon metal plates, and finally rubbed up into a fine powder in a mortar. The powder has a pleasant odor, and is almost tasteless. Twenty to fifty grams are stirred up in one-half liter of milk, and in this way about 100 gm. may be taken. Mosquera meat-meal is to be used in the same way.

Finkler's Tropon is easily assimilable, contains 90 per cent. albumin, and may be taken in quantities of 20 to 60 gm. a day in lukewarm milk, cocoa, soups, broths, or as zwieback.

Soluble powdered albumin. Of especial importance are the casein compounds, namely, eucasin (ammoniacal casein of Salkowski) and nutrose (sodium casein of Röhmann). Both are easily soluble, tolerably tasteless and odorless powders, which may be added to milk, soups, vegetables, cocoa, or wine, in quantities not exceeding three to five teaspoonfuls per day, or 50 gm. They are highly valued, and rightly so. If the patient is a drug-hater or sensitive, I add the preparations to his food without telling him. They contain 80 to 90 per cent. of albumin, *i. e.*, one teaspoonful, which equals 10 gm., 8 gm. of albumin, or 33 calories.

In case of hypochlorhydria it is desirable to introduce the albumin already digested into the stomach. This purpose is served by the *peptones*, and *propeptones* or *albumoses*, which are intermediate products of proteid digestion: Liebig's, Kemmerich's, Denayer's, Koch's peptone, somatose, etc. All the peptones in use contain a considerable percentage of albumose. Liebig's, or Kemmerich's peptones, taken two to four times daily, in amounts equivalent to 10 gm., in combination with bouillon, porridge, vegetables, sauce, or wine, contribute 3.5 gm. of absorbable albumin, and thus not only constitute a valuable source of nutrition, but also stimulate through their extractives. Somatose contains 8 gm. of absorbable albumin in 10 gm., but no extractives, and so does not stimulate the nervous system. The dose is two or three teaspoonfuls in soup, cocoa, or coffee; larger doses lead to diarrheas, and may therefore be used in case of constipation. Since in eucasin and nutrose we possess preparations which are not inferior to somatose, and are very much cheaper, the latter preparation is far less in demand.

Substances which contain gelatin protect the albumins of the body to a remarkable degree, as has been shown by the researches of von Voit. They are prepared from gelatin, calves' feet, etc., and, being variously flavored, afford a grateful change to those who suffer from anorexia and fever.

Fatty Preparations.—Experience has shown that the ingestion of large amounts of fats is of great value in phthisis. *Cod-liver oil* has long been esteemed, because it lends itself especially well to emulsification, and therefore to digestion and assimilation. One hundred grams equal 930 calories. The odor and the taste are disagreeable to most persons. In the hospital, however, I have a patient who has gained remarkably in weight, owing to the fact that he has for some time drunk the cod-liver oil refused by the eight other patients in the same ward. Children sometimes grow to be extremely fond of it. The taste may be disguised by adding lemon juice or rum, or by following it with peppermint tablets or burnt coffee beans, or by holding the nose, or by pouring it into the pharynx with a large spoon. *Praxis est multiplex.* The following formulas are used in the Brompton Hospital:

℞.	Ol. jecor. aselli	
	Aq. calcis	āā 100.0
	Saccharini	0.1
	Ol. menth. pip	gtt. 10
M.	Sig.—Three dessertspoonfuls daily.	

℞.	Ol. jecor. aselli	100.0
	Liq. ammon. fort	gtt. 10
	Ol. cinnamomi	gtt. 5
	Syrupi simplex	35.0
M.	Sig.—Three teaspoonfuls daily	

One begins with one or two teaspoonfuls, and increases the dose to three to six dessertspoonfuls (sometimes ten to fifteen) daily. It is best to give it one or two hours after meals, so as not to affect the appetite. The dark variety is considered more active, on account of its larger percentage of the fatty acids (6 per cent.). Cod-liver oil owes its importance chiefly to the fact that it is a cheap fat. Sesame oil, which is even cheaper and equally nutritious, has often been substituted for it. If the price does not enter into consideration, it finds a more agreeable substitute in lipanin, recommended by von Mering, which is composed of 94 parts of pure olive oil and 6 parts of oleic acid. It has a far more pleasant taste than cod-liver oil, has the advantage of being well borne in the warm seasons, and is easily digestible. Its dose is two to four dessertspoonfuls daily; each dessertspoonful is equivalent to 186 calories. The advantages of *cream* have already been indicated.

Artificial Carbohydrate Foods.—Especially important are *Knorr's nutritive meals:* oats, which are very rich in fats, rice, barley, oat-meal, shredded oats, peas, beans, and lentils, in the shape of meal; also the *leguminoses of Hartenstein,* which serve as a somewhat imperfect substitute for milk. They are based upon the attempt to facilitate the digestive process of saccharization, by reducing the substances to the finest possible powder. They may also be used for soups: 20, 30, or even 80 gm. of the meal are boiled with three-fourths of a liter of water or of water and milk, and to these soups meat extract may be added to improve the taste, or white of egg and peptone. They may be used as a substitute for or to alternate with breakfast.

Malt extract (Löfflund, and others): extract of germinating barley reduced to a syrupy consistency contains about 50 per cent. sugar (10 per cent. dextrinized), soluble starches, and 5 to 6 per cent. albumin. The pleasant taste makes it a favorite preparation for children. Dose: one or two teaspoonfuls three times a day. One dessertspoonful (20 gm.) contains 13.65 carbohydrate, 1.09 albumin, or 60 calories; in other words, almost as much as an egg.

Of less importance, but sometimes prescribed for the sake of variety, are the malt beers and Braunschweiger beer.

Honey. One dessertspoonful (75 calories) about equals an egg, and deserves more extended use. It is especially suited for breakfast and afternoon (buttered bread or sliced bread with honey). It also helps to prevent constipation.

Cocoa (oat-cocoa, acorn-cocoa), chocolate, and especially the Kraftchocolade of von Mering, in which the addition of free fatty acids to the cocoa fats renders them more emulsible and digestible, are rightly prized. Ten grams of chocolate are equal to 400 calories. Cocoa has the disadvantage of rapidly palling on one, in which case it may be temporarily displaced by porridges. Cocoa of oats and of acorns, and acorn coffee, are of service in diarrhea.

Special Methods of Forced Feeding.—Debove was the first to systematically employ forced feeding. In case of nervous patients with an unconquerable aversion to food, but with a normal digestion he would introduce by means of the stomach-tube (gavage) four to ten eggs, 200 gm. of meat powder, and 2 liters of milk. The food was digested, and the weight greatly improved. This forced feeding has been frequently tried—by Peiper, de Renzi, von Leyden—and with the best results. The disagreeable features of the method—the disgust and the accompanying disturbances of digestion—are so great, however, that the patient rejects it, and it can be employed only in extraordinary instances. In most cases the tube can be avoided by strenuous urging on the part of the physician.

Weir Mitchell's Method.—The patient is kept at absolute rest, physically and mentally, separated from his family and his accustomed environment, put to bed, and fed for the first four days on 100 cc. of milk every two hours. The dose is increased until the daily portion amounts to three or four liters. The milk must be taken very carefully and in swallows, so that, as Brehmer prescribed, $\frac{1}{16}$ of a liter is taken in a quarter of an hour. After a few days the diet is increased by the addition of white bread, potato purée, then roast meat, and finally vegetables, butter and bread, three times daily. At the same time active bodily exercise is replaced by massage of all the muscles (one-half to one hour twice daily) and general faradization (one-half hour twice daily).

Naturally, these methods are applicable only in case of nervous anorexia and dyspepsia in highly neurasthenic consumptives, the motor and chemical functions being completely intact.

With all due recognition of the value of a profuse or even excessive dietary in phthisis, it seems to me that the matter is occasionally overdone. Every stomach, no matter how strong, has its own limits. If overworked for any considerable length of time, especially if forced to manage large quantities of fluids (*e. g.*, milk), it may become paretic, atonic, and ectatic. It refuses food in every form. So we have escaped Scylla and fallen prey to Charybdis. It is evident that this accident may have the most serious consequences for the consumptive. Volland's warning against forced feeding is therefore in part justified, and should be taken well to heart. But when Volland counsels the physician to rely upon change of climate and rest in bed, and to wait until the invalid voluntarily demands food, he exposes the patient to no less a danger from the expectant treatment, since the patient may die while the physician is waiting. Indeed, it has been shown that often, as in nervous dyspepsia, only the desire is lacking, and the stomach actually pines for the food which the whim of the patient denies it. If food is put into the stomach, it will digest it.

Forced feeding is valuable up to the limits of the patient's capacity, and under close and continuous observation. As soon as the slightest disturbance manifests itself, the patient should be put upon fluid diet, or the stomach should be given absolute rest while nutrient enemata are made use of for two or three days. The appetite generally quickly returns. Then I give light diet for two or three days longer, and gradually return to the old régime.

For *nutrient enemata* the following formula is of service: The peptonized milk enema contains 250 gm. of milk (170 calories) and 60 gm. of peptone (100 calories), which equals 270 calories. The starch-milk enema contains 60 to 70 gm. of starch and 250 gm. of milk (Leube). Ewald recommends the following mixture: 2 or 3 eggs, ½ cup of 20 per cent. solution of grape-sugar, 1 glass of red wine, a thimbleful of starch; Boas: 250 gm. of milk, the yolks of two eggs, a pinch of salt, a dessertspoonful of red wine, and one of starch; Kemmerich's meat peptone may be added. All in all, 700 to 800 calories may be taken in—an amount which does not, indeed, suffice to satisfy the daily needs of the organism.

In order to insure the retention and absorption of the enema, it must be preceded by a cleansing enema, and should follow the return of this after one-half to one hour. The patient flexes his legs, and a long stomach-tube of rubber, lubricated with oil, is shoved as high as possible up the rectum. The irrigator is held about one meter high. The patient must try to retain the enema as long as possible, and lie quietly for at least one hour. If the rectum is very irritable, a few drops of the tincture of opium may be added to the enema, or a suppository of opium may precede it (extr. opii 0.05, but. cocoa 2.0).

Whey and Grape Cures.—*Whey* is obtained by removing the casein from milk. The mode of preparing it varies in different places, as does the value of the product. The whey cure, once highly esteemed, then looked down upon, has again sprung into favor. For many invalids it possesses undeniable advantages, which are not alone attributable to the change of climate and of surroundings. In many cases, however, the whey is not well borne, and leads to diarrhea. It is most valuable in the catarrhal conditions of phthisis, in combination with mineral waters, *e. g.*, the Arminius spring of Lippspring. I do not consider it necessary to prohibit the use of fats; on the contrary, I have employed forced feeding for the last eleven years, except in cases in which fats were previously not well borne, and have never observed any ill effects. The usual method is to give 200 gm. on an empty stomach. The chief resorts are: Reichenhall, Meran, Kreuth, Salzbrunn, Badenweiler, Reinerz, and many other minor places.

Of the *grape cure* essentially the same may be said. In the first place, it is suited only to invalids in an afebrile condition, with early processes, especially if they are constipated. In many cases it improves the appetite and the nutrition. The resorts in which the grapes have large, juicy, meaty pulps and thin skins are the best. The grapes must, of course, be ripe, and should be well washed and stripped of skin and pit. The beginning dose is $\frac{1}{4}$ kg., which is increased to 2 or 3 kg., rarely higher, on account of the danger of diarrhea. As a rule, one-half is taken in the morning on an empty stomach, one-fourth before dinner, and one-fourth before supper; others (de Renzi) give it after meals. It should be combined with a very nitrogenous diet. Especial care should be given to the teeth. Places in good repute for the grape cure, and also beneficial for consumptives, are Meran, Bozen, and Wiesbaden.

Alcohol.—Brehmer introduced alcohol (one gram equals seven calories) into phthisiotherapy. It saves the body-albumin, stimulates the appetite, in small doses hastens gastric digestion, facilitates the absorption of fats, and slightly lowers the body-temperature. The increase in the cutaneous circulation once led to the erroneous belief that alcohol raised the temperature. It also stimulates the heart and the central nervous system, and favorably affects the night-sweats and the sleeplessness. These qualities make it a valuable drug in many cases; they also furnish the indications for its use. It is to be regarded, not as an indifferent article of food, but as a drug the abuse of which may have the most terrible consequences for the patient. It is, therefore, extremely important to regulate the quantity and the quality exactly according to the needs of the patient.

If there is no especial indication the patient may be ordered a small glass (80 to 100 gm.) of strong southern wine in the forenoon, in order to stimulate the appetite. In case it fails of this effect, milk is to be preferred. In the same way, he may be given one or two glasses (of 120 gm.) of light red or white wine, according to the condition of the bowels, in the afternoon and evening. The southern wines have 15 to 18 per cent. of alcohol, and a considerable proportion of extractives; the lighter wines 8 to 10 per cent. The addition of eggs to the red wine or the cognac is both agreeable and nutritious.

The percentage content of alcohol according to König, Liebreich, and others, is as follows:

Moselle	8 to 12 per cent.	Port	16 to 20 per cent.
Rhine Wine	8 to 15 per cent.	Madeira	16 per cent.
Pfälz	9 to 12 per cent.	Champagne	9 to 12 per cent.
Hungarian, White	8 to 10 per cent.	Cider	3 to 10 per cent.
Bordeaux	8 to 14 per cent.	Munich Beer	3 to 4 per cent.
Tokay	12 per cent.	Porter and Ale	5 per cent.

In some cases, especially in the hot season, a glass of beer serves as a better appetizer (real Münchener, or heavy Culmbacher, Erlanger, or porter); there is no objection to its use. Beer has a good effect upon sleep in many cases.

If there is gastritis or a distaste for alcohol, it should be avoided except in the cases just mentioned. If it provokes cough, it should be followed by a drink of water, which controls it better than mixing it with the water.

The prescribed quantities should be exceeded only if the patient is very weak or in collapse. In this case, small doses (5 to 10 gm.) of fine cognac (50 to 55 per cent. of alcohol), brandy, whisky, arrac, rum (77 per cent. of alcohol), are indicated. The actual cognac cure,—70 to 80 gm. of cognac, in addition to a bottle of wine,—as advocated by Dettweiler, has been almost completely abandoned, since there is danger of the habit. A glass of milk with two teaspoonfuls of cognac is a good remedy against night-sweats that Brehmer has used.

Alcohol is a whip for the heart, and a whip should not be abused. The more sparing we are with alcohol, the better will it serve us in need, as in intercurrent pneumonia and at times in chills and fever. At such times, however, one should not fear to prescribe larger doses of the drug.

Children should have alcohol only when urgently indicated. In case of hemoptysis it should be discontinued for five to eight days after the cessation of the hemorrhage.

Other drinks, in addition to those already recommended, are milk of almonds (40 sweet and 2 bitter almonds with 20 gm. of sugar, crushed, mixed with 1 liter of water, and boiled; 620 calories to the liter, according to Hoffmann; very pleasant for occasional use); also buttermilk, tea with a good deal of cream, light apple cider with soda-water, and especially the fruit juices—notably currant wine. Egg-water and egg-albumin dissolved in water with milk are pleasant drinks, but particularly cold cocoa in milk, with or without vanilla.

AIR CURE.

Nourishment and air are therapeutically on a par. It is an old surgical observation that wounds exposed to an unclean, germ-bearing atmosphere easily fall prey to suppurative processes, which may constitute severe infections. The same holds true of the lung. The broken-down tissues and the temperature of the body offer far more favorable conditions than do external wounds, and it is only the inaccessibility of the alveoli which prevents every tubercle from becoming the point of development of such secondary infections.

Aside from bacteria, the air, especially in dwellings and when many people are together, contains a large number of gases, derived from the air of expiration, the perspiration of the people, from heating, cooking, etc., and these, in strong concentration, may become apparent and unpleasant even to the olfactory organs. It is well known that it is very disagreeable to live over a kitchen, that cooks and housewives, when they have provided the food for the family, often have little appetite themselves, and that an assemblage of men in a closed room destroys the appetite. A small admixture of noxious gases is not, indeed, perceptible to the senses, but has none the less an undesirable effect upon the appetite and the other bodily functions.

One of the fundamental requirements of phthisiotherapy, therefore, is the free enjoyment of pure air, and this must be satisfied to the full if the best results are to be obtained.

Miquel found, in one cubic centimeter of air, upon the observatory of Montsouris 80 bacteria; in the Rue de Rivoli, 920 bacteria; in the Hotel Dieu, 7500 bacteria; in the Hotel de la Pitié, 29,000 bacteria. The air of the ocean is almost germ-free (Fischer). Frankland's and Petri's researches have yielded similar results.

The air of closed spaces and of densely inhabited rooms is, then, by far the richest in germs. It is much less, but still considerably so, in thickly inhabited streets. It is least so ($\frac{1}{1000}$ to $\frac{1}{10000}$) in the open, far from large cities and centers, on mountains, at the seashore, and on the open sea. The same holds true of the dust and impure gases of the atmosphere.

Life in the country is not always synonymous with life in the open, and the conditions may not vary essentially from those in the city. It would, therefore, be an error to assume that the consumptive runs only $\frac{1}{1000}$ of the danger of a secondary infection in the country. (See the chapter on Infection.) Even in the country, proper hygienic conditions are furnished only by actual life in the open.

We are as yet unable to say whether the sunlight affects the organism by its chemical rays; the possibility has, however, been brought home to us by the discovery of the Röntgen rays. Its destructive influence over germs is well recognized, and tends, in part, to neutralize the danger from dust.

Physicians are still for the most part in possession of very vague notions regarding the management of the air cure, and it is, therefore, no wonder that they content themselves with such advice to their patients as "Walk a good deal." Such meaningless words often cause more harm than good. The invalid should not only go walking; he should spend the greater part of the day, or rather of his entire life, in the pure, open air.

There are, indeed, certain limitations to this requirement, which are to be sought less in the weather and the climate than in certain other conditions and in the idiosyncrasies of the patient.

"Favorable weather" comprises much more than merely fine weather. The consumptive derives benefit from the open air not only when it is sunny, dry, and the wind quiet, but no less when it is cloudy, damp, and the wind and rain are at work. There is, in fact, no basis for the assumption that cloudy skies are injurious—an idea which was previously instrumental, especially in southern resorts, in keeping patients indoors except in sunny weather. On the contrary, prolonged exposure to the heat of the sun, especially in summer, when the rays fall vertically, is in many respects injurious, and not rarely causes congestion of the head and lungs, and coughing of blood. The patient should protect himself to a certain extent from the direct heat of the summer sun, and should seek the shade.

Snow and rain do not forbid sojourn in the open. Indeed, the air is hardly ever clearer and balmier than during and after a storm. Even a moderate degree of fog is not harmful, unless it is saturated with coal and dust, as in cities. The invalid should, of course, be protected from being soaked by solid foot-wear, by waterproof cloaks, and, if necessary, by constructing a shelter.

The movement of the air is a factor of some moment in the air cure. When the fresh air is at rest, there are fewest germs in circulation, and even the presence of slight currents may, under certain circumstances, be prejudicial to the welfare of consumptives. Heavy winds are a double source of danger to him. In the first place, they rapidly abstract warmth from the body, and in this way may easily do harm to an individual whose temperature is already at an unstable equilibrium; this danger may be partially obviated by the hardening cure. Secondly, the wind carries dust and germs, which may irritate mechanically and infect the lung, a danger which there is no means of obviating. The east wind is especially feared by Germans, because the wind, having traversed wide stretches of arid country, has surrendered its moisture and is dry and piercing.

The temperature is, on the whole, not a factor of great importance. Warm climates were formerly considered favorable, and there is no doubt that some—the house-lovers and the very weak—feel better in warm air. On the other hand, consumption is an indigenous disease, and often rapidly fatal, in the warmer countries, *e. g.*, Italy, southern France, and Algiers. In cold Iceland, in the Faroes, in parts of Siberia, and in northern Norway, it is a rare and sluggish disease. Further, the German winter resorts with their low temperatures, and the mountain resorts, *e. g.*, Davos, attain results which compare favorably with those of the South. These facts prove that recovery is not very dependent upon the temperature. When I went to Görbersdorf from the University, I was shocked to find that consumptives were taking walks when the thermometer was at 12° C., but I soon convinced myself that this was productive of nothing but good.

Only rapid changes of temperature and sudden falls ordinarily affect the consumptive to any extent. In order to discount this source of danger timely provision of proper clothing must be made, and a well-planned course of hardening must be carried out. Consumptives often make the mistake of guarding against sudden falls of temperature by clothing themselves very heavily. The lengths to which they will go, especially in the poorer classes, surpass belief; a thick Jäger shirt, a flannel binder, a shirt, a corset, a corset-cover, a night jacket, and a blouse over all, is not a rare combination. This is a piece of folly which works in just the wrong way, by maintaining a constant sweat and so making the skin over-sensitive. For years I have advocated a mesh-garment (of either wool or silk) to be worn under the shirt, which does not unnecessarily irritate the skin, maintains a layer of warm air, furthers ventilation, and absorbs the sweat. In winter one may use a little heavier wool, and over it a shirt, vest, and coat; for women, a shirt which should not be too open, a comfortable corset, and a jacket.

For walks the long havelocks are the best, and the patient should always have one with him, in order to provide against sudden falls of temperature, rain-storms, or other accidents.

HARDENING.

In addition to caution and proper clothing, a course of hardening is very important.

If the patient is very sensitive, and it is winter, one begins with rubbings, morning and evening, and these should be carried on preferably by another person with French brandy, and salt. In this way the skin is cleansed of sweat, scales, and fat, and a pleasant feeling of warmth and well-being is induced. If his condition permits it, the patient rapidly completes his toilet after the rubbing and goes for his walk.

In place of the brandy, one may substitute the dry rubbings recommended by Dettweiler. The patient is put naked into a large coarse sheet, and then rubbed by an expert, who makes long quick strokes from head to foot and, if possible, brings a strong glow to the skin.

In a week or more the partial moist rubbing is begun. The patient lies in bed, and the various parts of his body are rubbed with a wash-rag wrung out of water at 66° to 92° F. until there is a ruddy reaction, and the patient is then covered again. After this, the patient rests for half an hour.

Later on, when the cutaneous vessels have begun to assume their normal functions, the full moist or wet rubbings are made use of with strong patients, especially in summer time. The patient is either taken directly from his bed, and given the treatment upon an empty stomach, although weaker individuals may be permitted a glass of warm milk or tea one-half hour before, or a short walk or dry rub precedes it, in order to induce a good reaction. The patient, entirely nude, is wrapped in a cloth wrung out (later wet) in 5 per cent. brine, at a temperature of 90° F. so that it comes into contact with the body all over, and is then rubbed by an experienced man, with long, powerful strokes, until there is an agreeable feeling of warmth over the entire body. A wet cloth may be laid on the head to guard against headache. The entire rubbing lasts hardly one to two minutes, after which the patient is laid in a dry sheet and again rubbed. He dresses without delay, and goes out into the open air for at least half an hour. After his walk he takes breakfast. Weaker patients get into bed for another quarter of an hour. The temperature of the brine is lowered one degree each day until it reaches 70°, 65°, or even 60° F. Winternitz uses only the lower temperatures, down to 45° F., and finds them neither unpleasant nor harmful. With this I am not in accord, since cold water is in many cases an actual torture. If the patient stands it, the temperature can be lowered.

The full rub is of great value, because the entire body is simultaneously brought to a lower temperature, exactly as is the case in rapid atmospheric variations or with draughts. The contraction and dilatation of the cutaneous vessels, which is here artificially induced by the cold pack and the subsequent friction, eventually follow as a spontaneous reflex, whatever the change in temperature.

It is very important that the full rub should be done quickly, energetically, and expertly. The patient should have a pleasant feeling of warmth; he should feel "as though newly born." If the treatment is followed by headache, discomfort, depression, and chilliness, this result is almost invariably to be ascribed to improper manipulation, assuming, of course, that the patient was sufficiently strong to stand the treatment. Skill on the part of the nurse is, therefore, a prime requisite. I rarely permit the relatives to carry out the treatment.

The douche, introduced by Brehmer into phthisiotherapy and subsequently greatly limited in its scope, represents a further step in the cure. Only very strong persons are capable of standing it, and it is best to have it done in the presence of the doctor. The duration should be gradually increased from five to forty seconds, the temperature should be from 90° to 95° F. or warmer. During the douche the patient must rub himself. After it, he is dried, dresses himself, and takes exercise in the air. Inasmuch as the douches induce forcible breathing, and may lead to the aspiration of sputum, they are to be employed only with the greatest care, and are absolutely excluded in very irritable cases and those with a considerable amount of sputum.

The rubs do not serve to cleanse the skin, and are no substitute for baths, which should be taken once a week at a temperature of 90° to 95° F. In the bath the patient is thoroughly soaped and washed, and rubbed off cool, and then dried. He is then given half an hour of rest. In cases of hemoptysis, one should be extremely cautious with baths, or should discontinue them entirely and substitute cleansing of each part of the body in succession.

These procedures serve not only to harden the body against variations of temperature, but also improve the appetite and nutrition, and favorably affect the mental conditions.

EXERCISE AND REST CURE.

One of the most important questions relates to the amount of exercise. If the patient is to spend the entire day in the open air, it is not a matter of indifference how he fills his time. Every motion costs the body albumin, climbing more than walking, walking more than sitting, and sitting more than lying down. The more quietly the patient lies, the less he moves his muscles, the less substance does he consume. If he suffers from consumption, all movement is to be closely limited. Moreover, the heart is seriously affected by the toxins, and if, in addition, extra work is put upon it, it is very apt to become paretic. Slight excesses of exertion betray themselves by an increased rapidity of the pulse, and greater ones by palpitation. Anemia, so frequently a complication of phthisis, also demands rest (Nothnagel). The absorption of toxins, which is indicated by the rises of temperature following upon exercise, is another cause for quiet.

If there are signs of progressive consumption and cardiac irritability, rest is the chief requirement. The advantages which the patient gains through the exercise—increased ease in expectoration, improvement of the appetite and the morale—are hardly to be considered. In order to combat the loss of appetite which comes from prolonged rest in bed, and also its ill effect upon the functions of the skin and muscles, we may make use of massage of the extremities, and even of the abdomen, but never of the thorax, for half an hour once or twice daily, or of faradization with the electrical massage roller, as is advocated by Binswanger, in combination with the Weir Mitchell cure.

The *rest cure* introduced by Dettweiler also fulfils the indication of rest in a satisfactory manner.

This cure demands certain very special arrangements. The invalid is brought into the open at the least possible cost of exertion, even being carried if necessary, and spends the entire day out-of-doors, in some place open toward the south and protected from the wind and rain, covering himself in summer with a light blanket, and in winter with a jacket and foot-muffs. As a reclining chair, I recommend a rattan chaise lounge with an adjustable back-rest, and with a horsehair mattress, if necessary (the Falkenstein-Honnef pattern). The chairs can be fitted with apparatus which makes it possible to read and write without exertion.

The patients are to be gradually accustomed to the continuous sojourn in the open air. Those who are unaccustomed to the open air become exhausted and wearied, like convalescents who get out into the open after a prolonged illness; but they rapidly become accustomed to it and appreciate its benefits, so that they can be brought to spend the entire day there. The spirits improve, and appetite, sleep, and respiration all get better. Often the physician meets with opposition not only from the patient, but also from the relatives; he should not, however, despair, and eventually he will earn the gratitude of his patient. After the habit has become established, the patient may be allowed to enjoy the fresh air until bedtime, *i. e.*, toward ten o'clock, except, of course, in bad weather or in malarial regions. At sundown the rapid fall of temperature is to be compensated by heavier clothing. Only rarely, especially in throat cases, is cough increased by the night air. Such must, naturally, retire earlier, but as a rule they rapidly accustom themselves to the night air. It is often an advantage if these patients accustom themselves to breathe entirely through the nose.

Pavilions, which may easily be turned to suit convenience, are also useful in the rest cure. If necessary, a suitable arbor may be constructed.

Suspended mats hem in the space too much. If the patient cannot be allowed to move about, a comfortable wheel-chair will serve to vary the monotony. In cool weather an occasional glass of warm milk is grateful.

The *amount of exercise* must be definitely specified. One begins with easy exercise, and limits the patient to ten to fifteen minutes every two or three hours, at first only on level ground. As soon as the forehead becomes moist, the pulse more rapid, or palpitation occurs, or rather before these symptoms show themselves, he should sit down. "The healthy man sits down because he is tired; the consumptive should sit down so as not to become tired." This was the old rule of Brehmer. The patient must be taught that all over-exertion is poison, and that he must never fix a predetermined amount of work, but that his feelings are at any time the only guide. Acceleration of the pulse, perspiration, palpitation, rise of temperature, feelings of weakness, discomfort and headache, are all signs that he has overstepped his limit of exercise.

Only when the body stands these little excursions without reaction, when the weight increases noticeably or maintains itself at a satisfactory height, can one permit an increase, although always under careful supervision, aided perhaps by a pedometer. If there is a notable increase in the adipose tissue, exercise is not only bearable, but actually necessary, in order to change the fat into proteid. There should be both slight grades and levels to choose from, and ample opportunities to sit down. Climbing is out of the question.

An exercise cure of this kind is the most satisfactory, and is the type to be followed. There are exceptional cases, which do not stand a quiet life well. They become morose, and anorexia, stoppage of expectoration, even hypostatic congestion, may occur. Of two evils one chooses the lesser, and gives them their liberty. One should, however, prescribe frequent intervals of rest for them.

It is self-evident that the consumptive cannot adopt the pace of the athlete, and that bicycling, rowing, and dancing are proscribed. Bowling and billiards are also too violent for him to indulge in. Only after the cure is complete are such games open to him.

Respiratory Gymnastics.—Respiratory gymnastics also fall within the subject of the fresh-air treatment. Since of old, consumptives have always been admonished to breathe deeply, on the theory that the air, the oxygen, the ozone, had a specific curative power over the tuberculous lung.

It is questionable, however, whether the improvement in the pulmonary circulation and the increased supply of oxygen to the lungs are actually beneficial. We know that an increase of oxygen favors the growth of the bacilli, and that pleuritic exudates, which lower the nutrition of the lung and thereby the rate of absorption of proteins, bring about improvement.

No surgeon advocates exercise of a tuberculous joint, especially forced exercise. The same principle must hold good for the lung. Indeed, the improvement in the pulmonary circulation is rather likely to increase the absorption of proteins, and to impede the formation of a zone of demarcation. The rise of temperature which follows upon forced breathing and muscular exertion may be regarded as evidence of this increased absorption. Furthermore, forcible, and particularly sudden, inspirations, such as form part of respiratory gymnastics, may occasion the aspiration of sputum into healthy parts of the lung and so set up secondary pneumonias. It is not without reason that relapses occur so frequently within a few days of some exhausting excursion.

The matter stands differently when the focus has become walled off, and no more sputum is produced. Then it is possible that a well-regulated course of respiratory exercises may be beneficial.

For years I have absolutely banished forcible inspirations in the form in which they are usually prescribed, regarding them as nothing less than dangerous and harmful. I prefer to advise the patients to breathe in *slowly* and not too deeply, and then to breathe the air out again without effort, in order to further the removal of the products by expectoration. I myself, and, what is of no less importance, my patients, are perfectly satisfied with the results. Brehmer, Volland, and Liebermeister long ago gave warning against the dangers of pulmonary gymnastics.

MENTAL OCCUPATION.

Rest of the mind must go hand in hand with that of the body. The physician has need of foresight and of tact to hit the needs of his patient right. Every form of excitement is to be avoided and relatives and nurses are to be admonished of this. Those who are excitable or melancholic demand diversion in the form of light reading. Best suited to this purpose are works of history or travel, or humorous papers, according to the intelligence of the reader. Sensational romances and novels of crime are excluded. Cards, chess, and the piano are best prohibited; eager players are certainly harmed by the excitement. Many institutions are too lax on this subject. Best adapted to the purpose are gentle indoor games not played for money, collecting stamps, plants and coins, photography, and other innocent amusements. As soon as the strength permits, however, I consider it the moral duty of the physician to find some suitable occupation for his patient. Nothing is so deleterious to a subsequent career as years of invalidism spent in institutions and health resorts.

HYGIENE OF THE DWELLING.

Indoor life is, indeed, to be limited as far as possible, but cannot be entirely avoided. At night and in stormy weather the patient is confined to his room, and intercurrent relapses, fever, and hemorrhage keep him in bed. Under such circumstances, however, he should at least be given the benefit of fresh air.

The *room* should be large, airy and sunny, and, if possible, with a southern exposure. The bactericidal action of the sunlight has been repeatedly mentioned. Everything which tends to promote dust,—carpets, with the exception of the bed-rug, unnecessary cushioned furniture, curtains, etc.,—unless absolutely essential, is to be removed from the room. The floor and furniture should be cleaned in the morning, with the window open. The patient should leave the room, or, if this is impossible, should at least hold a cloth before his nose. These petty details are not beneath the notice of the physician, for they may easily become the source of danger which not even the best medicine can cure.

The window should be kept open; if there is an upper casement, it should hardly ever be closed. It is well, also, to have an arrangement for fastening the window at any desired level. Even at night the window may remain at least partially open, provided that the patient has been somewhat inured by the hardening process already described. The bed should have rollers, should be in a place free from draught, and should be moved to the window during the day. A screen should be used to protect the patient against sudden changes of temperature during his sleep at night. If there are two rooms, the window in the one adjoining should be kept open all night. The air becomes very heavy if the windows are kept closed, as one may discover by the odor which permeates the sleeping-room in the early morning. If the air is kept in circulation, these gases are constantly removed and the atmosphere remains pure; sleep is sounder and more refreshing, and the night-sweats are relieved.

It is desirable to have a balcony in connection with the room, to which the patient can have access at any time without exertion. This should be firm, covered, roomy, protected by glass walls from wind and rain, and by awnings from too fierce a sunlight. In this respect, as various authors have pointed out, the different health resorts and institutions are equally deficient. Even though the invalid is confined to his bed and cannot get to the general reclining room, there is no reason why he should not have the benefit of the fresh air on a protected balcony. A common balcony for the use of several rooms is to be condemned, unless it is partitioned off; I have known of several cases in which it served to promote sexual intercourse among the patients.

VOCATION.

In connection with the measures above described, it is assumed, of course, that the invalid gives up his calling for some length of time, even though his strength appears to justify him in following it. The physician must not, however, make demands which the circumstances of the patient render it impossible for him to follow. This is unnecessary, and embitters and harms the patient. The physician must ascertain from him to what extent his means permit of a prolonged rest, and should frame his demands accordingly. First inform yourself, then command. In acute cases it is naturally absolutely necessary to abandon work; such is, however, not the case if the disease has been chronic for some length of time, or if apyrexia and a steady maintainence or increase of the body-weight denote quiescence of the process.

Much depends upon the character of the calling. The more exertion, excitement (stock exchanges, etc.), anger, or dispute it involves, the more harmful it is. Such vocations as are associated with confinement in close, dusty rooms, factories, or mills are most dangerous, while file-cutting and glass-cutting are not to be considered.

LIMITATIONS DUE TO PECUNIARY CONDITIONS.

Our desires often meet with insuperable obstacles owing to the financial condition of the invalid. This multiplies our difficulties, but by no means condemns us to inaction. We should always keep in mind the fact that the material of autopsies, the bodies of the poor, show healed foci.

The dietary may be simpler, and yet efficient, if only meat, fat (oils, preferably butter, fried bacon, cod-liver oil), milk, eggs, and porridges are procurable in sufficient quantities. A good whisky or Nordhäuser in small quantities with milk may be substituted for cognac and wine.

It is more difficult to comply with the indication for fresh air. We must see that the invalid gets out of his business surroundings as soon as possible, especially if they are harmful and the probable source of his infection. He should select a dwelling which lies fairly free and is not too high, perhaps in the neighborhood of some park, so that he can easily get fresh air. We should interest ourselves in the dwelling conditions, and should suggest little changes for the benefit of our patients. We may at least be able so to arrange matters that our patient has a room to himself, perhaps one fronting on the street or a wide court. The window should be kept open as far as possible, and there should be scrupulous cleanliness.

All this takes much time and trouble, and the physician who is hampered by the difficult conditions of a sick fund practice, with all possible good-will and humanity, may well find it physically impossible to accomplish it. For such cases, national sanatoria, such as will be described below, are a crying need.

HEALTH RESORTS.

The conditions demanded by a rational treatment of the disease are rarely satisfied in the home, even in case of well-to-do people.

Far back in antiquity consumptives were sent to reputed health resorts.

Which cases should be sent away, where to, and for how long a time?

For cases in which the therapeutic indications cannot be satisfied in the home, and which have sufficient means, a change to a health resort is very desirable. The extent of the disease enters into account in so far that patients who have had high fever for some time, who are much emaciated, and who have no hope of recovery should not be subjected to the disturbances of a long journey with its unavoidable excitement and injury. It is just such patients who, on the approach of death, are seized with the desire to travel, although they had, perhaps, opposed that very demand when made by the physician in the earlier stages of the malady. It is difficult to dissuade them or to restrain them until "they shall be stronger."

Fever in itself is no contraindication, even if it is high, if it has lasted only a few days or weeks, or if it has lasted for some time, but has not reached a very high point. It is, indeed, well recognized that change of climate often of itself rapidly cures fever. We must not throw up the sponge too early, for often patients have been saved by a change of environment after having been given up.

There is a general tendency to wait until the fever has abated. I, in common with many of the most experienced specialists, put faith in the favorable effect of a change, and take just the opposite standpoint. Nothnagel considers change of climate to be often the only cure for fever, and Brehmer and others similarly express themselves. The annoyances of a trip are to be recognized, but not overestimated; otherwise, it would be like postponing the use of antipyretics until the fever has abated.

On the whole, the patient is to be sent away as soon as possible. The sooner he goes, the better are the prospects for an early and complete recovery. Every week of delay may add months of invalidism. Nothing is so harmful as the notion that the patient is not so sick as to need immediate change, and that it is as well to wait. When once the diagnosis has been made, the disease is serious enough to make every delay injurious. Even if there is only a strong suspicion of tuberculosis, it is better to be on the safe side. It is preferable to send a patient away too early or unnecessarily rather than to have subsequent misgivings.

The patient often does not appreciate the necessity for the journey and makes all sorts of excuses: "He can't get away, he can't travel, his business will not permit it," etc. The relatives, too, out of ignorance, cupidity, fear of annoyance to themselves, or even worse motives, meet us with active or passive opposition. The physician often needs all his authority and energy to help him perform his duty. If he fails to insist upon his demands, he cannot avoid the reproaches of a subsequent disaster. He should, of course, carefully probe all objections, and estimate the pecuniary sacrifice involved. How often it happens that a patient who could "not afford" to go to a sanatorium has had to sacrifice ten times as much later on, and without avail.

Many a one, accustomed to live at home, fears the idea of leaving it, of being sick among strangers. But this can be overcome by logic, by an appeal to common sense and the love of family, or other suitable arguments.

The more unfavorable the hygienic conditions of the home, the more they harm the patient and wear upon his peace of mind, so much the more categorically should we insist upon his departure. But even if all the therapeutic indications can be fulfilled at home, we should still not undervalue the favorable influence which change of climate exercises upon the appetite and nutrition, and which new surroundings and country life have upon the spirits and the entire attitude of the patient.

It cannot be denied that, under the uncertain conditions which hedge about the success of a physician, there is need of all the nobility of our profession and a full recognition of its lofty social ideals to bring one to send away patients who are the wealthiest in his clientele, perhaps for months or years. Penzoldt is very likely in the right when he says that advantage would be more generally taken of the institutions and health resorts were it not for the inroads upon the personal resources of the physician which such advice implies. On the whole, however, this cause operates but rarely.

The physician must, therefore, conscientiously determine whether the home offers that combination of conditions most favorable to recovery, and whether he can rely on the execution of his orders, or, on the other hand, whether the chances of recovery are better away from home. He must decide the treatment.

Having once determined to send the patient away, are we to send a companion with him? If he has occasionally high temperatures and hemoptyses, or is confined to bed, it is, of course, desirable. The same holds true of those who are very much attached to home, for the psychical depression consequent upon leaving it may be very great, sufficient even to imperil the success of the treatment.

As Heinzelmann has excellently pointed out, the choice of a companion demands great care. It will not do to accept the person who is least in demand at home. One who is hard of hearing or too vivacious is just as unsuitable as a pleasure-seeker or a fat individual who wishes to reduce by exercise. Worrisome or sentimental persons are a plague to the patient. Bad children are to be left at home. Young and voluptuous wives should not accompany their husbands, and, similarly, a healthy husband is often the worst possible companion for his wife. As a rule, a relative finds it tedious, and puts up with less exercise than he requires only to demand more than is well, on his part, from the invalid. It is generally best, then, to select some competent and reliable stranger. It is just at the commencement that the choice of a room and other annoying arrangements make the presence of an intelligent and unselfish companion desirable.

WHERE SHALL WE SEND THE PATIENT?

Formerly this or that climate was especially lauded for consumptives. The literature is voluminous, but lacks the evidence of scientific observation. At one time it was a warm climate, at another a cold, or, again, a high altitude, which was regarded as of most value.

To-day we rightly regard no one climate as specific. Tuberculosis occurs in the warmth of the south as well as in the colder north and upon lofty plateaus. Recoveries, too, are seen in every clime.

The modern hematological methods have demonstrated an increase in the red blood-corpuscles proportional to the altitude (Viault, Egger, Jaruntowski and Schröder, Wolff, and others). Wolff went so far as to claim a revolution in the constitution of the blood, which completed itself even at moderate altitudes within a few days (eight to ten), and was to act specifically upon pulmonary diseases.

A number of hypotheses were constructed to account for this blood condition. Many authors assume an actual increase of the red cells, determined either by a prolongation of their lives (Fick) or by a real multiplication of their number (Miescher, Egger, Schaumann, Rosenquist). According to others, the increase is only apparent, and is attributable to concentration of the blood (Grawitz), or to vascular constriction and expression of the plasma into the lymph-spaces (Bunge). Some suggest that the corpuscles normally stagnant in certain organs are hurried into the general circulation; others, again, that there is an unequal distribution of the blood within the vascular system, due to nervous influences and variations in the blood-pressure (Zuntz). Gottstein's theory, that the increased count is due simply to an alteration in the cubic content of the counting chamber brought about by the diminution in atmospheric pressure, is scarcely probable, since it fails to account for the progressive increase of the corpuscles and also for the fact that it persists even though the count is made in the laboratory, in an unrarified atmosphere. Further investigations are needed upon this point.

The fact that tuberculosis is so rare in the mountains is due primarily to the absence of overcrowding, which is one of the chief factors in infection. I believe that there are also other factors at work. The rareness of the air tends to diminish the distribution of germs both indoors and out. This difference amounts to but little in any individual case, but in the aggregate serves to diminish the chances of infection both by the tubercle bacilli and by secondary bacteria.

Even though the character of the climate is no longer invested with its former importance, it does not follow that all climates are to be considered of equal value. Our knowledge upon this point is largely hypothetical. The essential factor is the amount of time which any given climate permits the patient to spend in the open air. The more he is confined indoors by rough weather, wind and storm, the less benefit does he derive.

The geological features may also make a place unsuitable for consumptives; *e. g.*, friable limestone foundations, which produce large quantities of dust.

Other climatic factors—rarity of the atmosphere, sunlight, humidity, etc.—are of less importance. The ozone content is given far more emphasis in the prospectuses than our present knowledge warrants.

Nevertheless, it is advisable to group the climates which enter into consideration into certain general classes.

A distinction is made between inland and sea climates.

INLAND CLIMATES.

These may be considered, according to the height above the level of the sea, as—

Climate of the Lowlands and of Levels under 400 Meters.—This makes very moderate demands upon the regulating mechanism of the body, but, on the other hand, is least stimulating to the appetite, the cutaneous functions, and the nervous system. Large bodies of water in the neighborhood, which render the atmosphere equable and moist, mountains and forests, which give protection from the wind, often make these climates very valuable. In a completely closed valley the temperature is very slowly equalized, and the deficient ventilation makes it somewhat oppressive in summer.

Such places for the summer are:

Lippspringe (Westphalia), 140 m., alkaline earth springs. Station Paderborn (Berlin-Aachen).

Rehburg, 100 m., alkaline earthy springs. Station Wunstorf (Post) and Lindhorst. Bremer, health resort for lung cases among the poorer classes (management in Bremen).

Salzungen (Thüringen), 262 m., brine baths, resort.

Soden on the Taunus, 140 m., sodium chloride springs. Höchst Soden, one-half hour from Frankfort-on-the-Main.

Sodenthal in Spessart, 143 m., iodin drinks. Station Sulzbach-a.-M.

Bad Ems, 82 m., alkaline chlorid springs.

Gleichenberg (Steiermark), 300 m.

Wiesbaden, 117 m., sodium chlorid hot springs.

Baden-Baden, 200 m., sodium chlorid hot springs.

Bad Liebenzell in Württemberg, 340 m., Station of the Horb-Pforzheimer Road.

Berka a. d. Ilm, near Weimar, 275 to 330 m. Waldschlafhütten, house for convalescent pulmonary invalids.

Honnef on the Rhine, at the foot of the Siebengebirges.

Hornberg, 380 m., also a winter resort, on the Black Forest Road.

Tabarz in the Thüringian Forest, 400 m., Station Fröttstädt on the Thüringian Forest Road.

Southern winter resorts, suitable also for late fall:

Arco, 90 m., grape cure. Mori-Arco, fairly free from wind and dust, except in September, October, and April.

Meran, in South German Tyrol, 319 to 520 m., grape cure. Bozen-Meran, windy at times, especially in autumn. The careful nursing is very praiseworthy.

Gries by Bozen, 275 m. above the Adriatic, grape, whey, and climatic health resort. Very pleasant, especially in autumn and spring, but the protected walks are rather short.

Montreux on the Genfersee (Canton Waadt), 380 m., spring, autumn, and winter resort. Air and grape cure. Road, Lausanne-Montreux-Brigue (Simplon). Boat, Geneva-Lausanne-Montreux-Bouveret.

Pallanza on Lake Maggiore (Upper Italy), 193 m., autumn, winter and spring. By steamboat from Laveno, Luino, Locarno. St. Gotthard route.

Locarno on Lago Maggiore (Switzerland), 204 m., autumn, winter, and spring. St. Gotthard route.

Lugano (Southern Switzerland), 275 m., often very windy. Station Riva on Lake Garda, often very windy.

Gardone Riviera on Lake Garda, often very windy, 70 m.

Fasano on Lake Garda, ten minutes from Gardone, well situated.

Arid climate, dry and warm:

Helouan, 57 m. above the average level of the Nile. Warm sulphur springs. North-German Lloyd to Port Said.

Luxor, three and one-half days from Cairo.

Assuan, five and one-half days from Cairo.

The Climate of Levels 400 to 950 Meters above the Sea.—*Mountain and Subalpine Climate.*—The increased altitude is, in general, associated with greater variations in temperature. There is greater stimulation of the nervous system, the appetite is improved, metabolism is increased. The air is clear and sterile, and there is generally more wind than at lower levels. The effect is tonic, but not too actively. If these altitudes are within the zone of high mountains, *e. g.*, the Alps, the variations are even greater. In the evening the mountain breeze rapidly lowers the temperature. The places are mostly fitted for summer occupation, but could be made suitable for winter residents.

In the Bavarian Mountains are:

Reichenhall, 470 m., brine baths, whey cure, reached by the Munich-Salzburger road, route: Paris-Vienna.

Kreuth, 850 m., Gmund on the Tegernsee, Jenbach and Achensee.

Berchtesgaden, 575 m., brine baths, summer resort and air cure. Reichenhall-Berchtesgaden (Munich-Salzburg).

Partenkirchen, 722 m., often windy. (Munich-Partenkirchen.)

In the Austrian Salzkammergut:

Ischl, 469 m., station of the Kronprinz Rudolf Road and Salzkammergut local road.

Gmunden on the Traunsee, 422 m.

Aussee, 650 m., iodin and bromid baths, brine, whey cure. Station of the Salzkammergut local road.

Further:

Ueberlingen on the Bodensee, 410 m.

Badenweiler, 452 m., hot baths, tramway to Mühlheim (7 km.) (Badische Staats Railway).

St. Blasien in the Bavarian Black Forest, 800 m., summer and winter, Hauff's sanatorium (now Dr. Sander's).

Triberg (Black Forest), 700 m., central station of the Schwarzwald road.

Sulzburg in the Bavarian Black Forest, about 450 m., Transients. Station.

Schluchtsee (South Bavarian Black Forest), 952 m., hilly country. Half-way station to and from the mountains.

Andreasberg in the upper Hartz, 620 m., very uneven country.

Friedrichsroda in the Thuringian Forest, 450 m.

Oberhof in Thuringia, 810 m., summer and winter resort. Station of the Neudietendorf-Ritschenhausen road. (Not for cases with fever.)

Reinerz (Silesia), 568 m., iron springs. Station Rückers-Reinerz (Breslau-Mittelwalder and Niederschlesisch-Märkische mountain railroad), or Nachod, 20 km.

Landeck (Silesia), 450 m., warm sulphur springs, resort.

Lavey-les-Bains (Canton Waadt), 433 m., warm sulphur springs. Station St. Maurice (Lausanne—Brigue—Simplon).

Heustrich (Upper Berne), 702 m., cold sulphur springs. Station Spiez (omnibus three-quarters of an hour).

Weissenburg in Upper Berne (Switzerland), 890 m., alkaline earth springs. Station Erlenbach, one hour.

Bürgenstock near Lucerne, on the Vierwaldstättersee, 870 m.

Flühli in the Entlebuch, 900 m. Schüpfheim (Berne-Lucerne).

Gersau on the Vierwaldstättersee, 440 m.

Interlaken in Upper Berne, 568 m.

Sonnenberg on the Seelisberg on the Vierwaldstättersee, 845 m.

Institutions for Pulmonary Invalids:

Görbersdorf in the Silesian Riesengebirge, 561 m.

Falkenstein on the southern spur of the Taunus, 400 m.

Schömberg (Württemberg Black Forest), 650 m. Station Liebenzell or Höfen.

Reiboldsgrün, about 700 m. Station Auerbach and Rautenkranz.

Mountain Climates (over 950 Meters).—Here the effect of the diminished atmospheric pressure upon pulse and respiration becomes strikingly evident. The air is cold. The sunlight, easily piercing the rare air, seems more intense. The difference of temperature between sun and shade, and day and night, is enormous. Changes of temperature occur with great suddenness. The humidity is absolutely, and generally also relatively, very slight.

In winter there is less agitation of the pure and sterile atmosphere and changes of temperature occur less suddenly. The circulation of the skin and lungs is improved, the loss of heat and moisture increased, respiration made fuller, and the appetite and state of nutrition generally ameliorated. The total effect is far more pronounced than at the middle levels, but the strength and resistance of the patient are also much more severely tested.

Winter and Summer Resorts.—Davos-Platz, much dust and wind in summer, and little shade. School sanatorium. Zürich-Landquart-Davos or Bodensee-Landquart-Davos. Especially for winter; recently much smoke in the lower villas.

Davos-Dorf (Canton Graubünden in Switzerland), 1574 m.

Les Avants, 1000 m. Two posts daily for Montreux.

Arosa (side valley of the Schanfigg in Graubünden), 1840 m., the hotels surrounded by hemlocks. Seven hours from Chur by carriage.

Leysin (Canton Waadt), 1264 m.

St. Moritz (Dorf), 1767 m. Iron springs. Next stations to the north (Switzerland) Chur, Thusis, Davos; to the east and southeast (Austria) Landeck and Meran; to the south and southwest (Italy) Chiavenna and Sondrio.

Samaden (Upper Engadin), about 2000 m.

Summer Resorts of the Higher Altitudes.—Seewis in the Prätigau, 1000 m., spring and autumn. Station Seewis of the Landquart-Davos road.

Grindelwald (Canton Berne), 1046 m.

Engelberg (Canton Unterwalden, Switzerland), 1019 m.

Gossensass on the southern spur of the Brenner Pass, 1100 m. Recently a winter resort. Austrian Southern Railroad.

Lenk (Canton Berne), 1105 m. Sulphur baths and air cure. Station Erlenbach.

Beatenberg above the Thunersee, 1148 m.

Rigi-Klösterli, 1317 m. Gotthard road to station Arth-Goldan, then out to Rigi-Klösterli.

Mendel near Bozen, 1354 m.

Madonna di Campiglio in Indicaria, 1515 m.

Mürren (above the Lauterbrunnen valley), 1650 m.

Pontresina (Upper Engadin), 1800 m.

Maloja Palace-Hotel (Upper Engadin), 1800 m. Station Thusis over the Julier or Albula Pass (Germany, England, France); Landquart over the Flüela Pass (just beyond). From Austria: Landeck via Tarasp. Gotthard route via Lecco-Chiavenna.

SEA CLIMATES.

Coast and Island Resorts.—These are characterized by high atmospheric pressure, strong winds, and freedom from dust (unless the streets are badly kept). The water maintains an even temperature and saturates the air with salt.

This climate affects the body markedly, stimulates the nerves, increases appetite and metabolism. Weaker individuals may suffer at times from anorexia, sleeplessness, and even hemorrhages.

Southern Winter Resorts with Sea Climate:

Moist.

Teneriffa, the Canaries (Spanish), the Azores and Madeira (Portuguese), suitable for prolonged stays.

Moderately Moist.

Riviera di Levante: St. Margeritha, Nervi, then Pegli (near Genoa), Corfu (Greek) in the Ionian Sea.

Ajaccio in Corsica. Ships to Leghorn, Marseilles, Nice, Bone.

Nervi, 10–15 m., free from dust only on the beach. Station on the road to Genoa-Pisa-Rome.

Malaga (southern coast of Spain).

Abbazia on the Adriatic. Winter resort, and sea bathing. Spring and autumn resort. Station Abbazia-Mattuglie (southern road).

Lussinpiccolo, island of Lussin near Pola, slightly windy.

Dry.

San Remo, much German spoken.

Mentone. One hour from Nice. Riviera di Ponente; the southern portion especially protected (Garavan).

Cannes (southern France).

Ospedaletti ligure, between San Remo and Bordighera.

Monte Carlo (unsuitable on account of the gambling).

Bordighera (Italy), last station in Italy. Somewhat windy.

Nice, beautifully situated. Better suited for amusement than for health; rather for the Parisian demi-monde than for the consumptive.

Capri near Naples.

The North and East Sea baths, which demand considerable strength.

Misdroy (on the Baltic), also a winter resort. By ship from Stettin (three hours), or from Wollin or Swinemünde by carriage (one and one-half hours).

Norderney on the North Sea, east Friesland, steamer from Norddeich (thirty to forty minutes), Bremerhaven, Hamburg. Winter accommodations.

Sylt (Westerland and Wenningstedt, Baltic). By ship from Hamburg or Hoyersschleuse.

Wangeroge (Baltic). Through Bremen, Oldenburg (eastern Germany) Münster-Osnabrück-Carolineninsel (western Germany).

Sea Journeys.—

[Among the climatic resorts in the United States commonly used for the treatment of pulmonary tuberculosis are the following:

Sea-coast Resorts.—

Mt. Desert, Maine.

Atlantic City and Cape May, New Jersey.

Old Point Comfort, Virginia.

Jacksonville, St. Augustine, and Palm Beach, Florida.

Monterey, Santa Barbara, Coronado Beach, San Diego, and Catalina Island, California.

Inland Resorts up to 1200 feet Altitude.—

Moosehead Lake	Maine	1000 feet
Sharon	Massachusetts	350 “
Lakewood	New Jersey	100 “
Camden	South Carolina	200 “
Aiken	“ “	550 “
Thomasville	Georgia	300 “
Augusta	“	150 “
San Antonio	Texas	350 “
Phœnix	Arizona	1100 “
Yuma	“	1400 “
Los Angeles	California	330 “
Pasadena	“	900 “
Riverside	“	850 “
Indio	“	50 “ below sea-level.
Salton	“	360 “ “ “

1200 to 3000 Feet.—

Rangeley Lakes	Maine	1511 feet
Bethlehem, White Mountains	New Hampshire	1459 “
Saranac Lake	New York	1600 “
Lake Placid	“ “	1860 “
Sharon Springs	“ “	1350 “
Liberty	“ “	2300 “
Asheville	North Carolina	2250 “
Redlands	California	1350 “
Tucson	Arizona	2400 “

3000 Feet and Higher.—

El Paso	Texas	3700 feet
Boulder	Colorado	5300 “
Denver	“	5300 “
Colorado Springs	“	6000 “
Manitou	“	6300 “
Pueblo	“	4700 “
Glenwood Springs	“	5200 “
Cañon City	“	5300 “
Salt Lake City	Utah	4300 “
Springer	New Mexico	5700 “
Las Vegas	“ “	6700 “
Santa Fe	“ “	7000 “
Albuquerque	“ “	5000 “
Silver City	“ “	5800 “
Fort Bayard	“ “	4450 “
Prescott	Arizona	5300 “
Flagstaff	“	7000 “ —Ed.]

FACTORS IN THE CHOICE OF CLIMATE AND PLACE.

It is evident that there is no dearth of places which are recommended or recommend themselves for consumptives, especially in Germany, Austria, Switzerland, and southern France. These places, however, vary enormously in value, and do not equally answer the demands of a rational cure. These are:

1. Protection from the wind, and freedom from dust, which depends partly upon the soil and partly upon the wind.

2. Good hygienic conditions; good spring-water, a proper system of water-supply, efficient sewerage system, drainage, street-sprinkling, disinfection, and the enforcement of prophylactic measures. A health resort is entitled to the name only if it satisfies all these requirements in the broadest sense.

3. Walks which are shady, well kept, in part level, in part of a moderate or steep grade, and of a goodly number, so that the patient does not soon weary of them. Opportunities to rest at any minute. Brehmer had a bench at every 20 paces of his 3½-mile walk.

4. Good, comfortable, bright houses (villa system), so that the patient can pursue the rest cure either at home upon a well-protected balcony or in a properly fitted garden. A shady path from the house to the woods.

5. Wholesome, palatable, varied diet.

6. Skilled attendance, in case of an intercurrent relapse. Unfortunately, it is often either entirely lacking, or is relegated to old women, who are unsuited to any other work.

7. Postal and telegraph connections, or, still better, a telephone.
8. Last but not least, an experienced physician.

It is self-evident that large cities are not suitable as health resorts. Nevertheless, even the later works continue to recommend such places as Pisa, Florence, Venice, Rome, Spezzia, and Cairo. I doubt whether the authors are personally acquainted with these places, with all their wind and dust, and their unhealthful dwellings. Only a very few houses comply with the requirements of hygiene, and these are not apt to fall into the hands of a stranger. Moreover, the mode of life is generally unsuitable. We send patients away not to study art, but to enjoy the fresh air. Such places do not sufficiently satisfy this demand, and the cold, draughty museums, with all their attractiveness for the cultured, are actually an objectionable feature. Prolonged sojourns and frequent visits have taught me to limit the choice of places far more narrowly.

The so-called summer and winter resorts which are characterized only by the beauty of their situation are usually unsuited for consumptives. By good luck the results are occasionally beneficial. The advantages of these summer places—their nearness, cheapness, and the absence of other consumptives—are not essential. Distance, with our modern traveling facilities, is not to be considered in so serious a matter as consumption, and the slight saving does not compensate for the diminished chance of recovery. It is an error to believe that the chance of infection is any smaller, since other patients will resort thither for the same reasons. The difference from a health resort lies in the neglect of precautionary measures against infection. Hygienic arrangements, drainage, water-conduits, protection against wind and rain, are all lacking, because not profitable. The nursing is often very primitive, the menu monotonous. There is often no physician near at hand, and no druggist. The physician should at least ascertain these conditions before sending his patient there.

The prospectuses of such places, which come to us in increasing numbers, are as a rule too optimistic. Since the infectiousness of phthisis has been more strongly emphasized, many places which previously proclaimed their value in all stages of the disease vie with each other in the assurance that they are suited especially or exclusively for early cases, for those without fever. Or they substitute such euphemistic expressions as chronic pulmonary catarrh, chronic induration of the lung, or apical catarrh. In the Bäder almanac only four places claim to be suited for all forms of phthisis. One place on the Riviera di Levante invites cases of "dry catarrh, with irritative cough, and a tendency to hemorrhage," and humorously adds that "consumptives with profuse expectoration belong rather in the Riviera di Ponente." The prospectuses, indeed, would offer us no choice of places to which to send our consumptives with fever—and most of them do occasionally have some elevation of temperature.

One could afford to overlook this matter, were it not for the very serious fact that the places consider themselves exonerated from precautionary measures on the ground that "no consumptives come there"; rather should they seek to excel themselves in this. Even where prophylaxis is claimed, it is often of a very primitive description. The nursing, too, is extremely deficient in many places, not excepting the institutions; there is routine procedure without individualization according to the needs of the patient.

The choice of a suitable climate for each case is often very difficult. It should be guided by the personality of the invalid, and the extent and previous course of his disease. The following general rules may be suggested: Cold, dry, and *rarefied air* stimulates strong individuals, increases the appetite, also at times the cough; in weakly, feverish consumptives it occasionally interferes with sleep and appetite. Hot climates depress, especially if associated with much moisture. Moist air facilitates expectoration.

In order to guard against subsequent disappointment and discontent, it is well to warn the patient that there are windy days in the most sheltered localities, days which will oblige him to keep to the house. An ideal climate does not exist; every place has its failings, and we can only select the best.

For weakly persons, therefore, and in proportion to the extent of their lesions, one prefers a mild, only slightly stimulating climate, such as the low-lying and subalpine regions (up to about 900 m.) offer in the warmer season of the year. This is a preparation for the more trying climates of the high mountains and the sea.

The choice of place depends upon the previously mentioned qualifications (position, hygiene, accommodations, etc.).

If I name Reichenhall as the place which my own experience leads me to consider as best suited for patients of this class, I hope it is not from the prejudice due to thirteen years of service in the place.

The climate of Reichenhall is very mild and yet stimulating, it is very free from dust and wind, and the valley is sufficiently broad to escape the reproach of being a "kettle-valley."

The rainfall is ample, and the ground rapidly absorbs the moisture.

Well-kept walks of every grade, with resting-places and a rich assortment of therapeutic apparatus (Penzoldt, von Ziemssen) are supplied: brine baths, hydrotherapeutic appliances. The requisite prophylactic measures are well carried out. It is excellent for diseases of the throat. For very nervous individuals I would recommend it, on account of the balmy air, only during spring and autumn.

Further, I have seen excellent results from Ems (poor prophylaxis), and from Gleichenberg (both having very good appliances for inhalation). In the former the narrowness of the valley renders the air very oppressive in summer. Badenweiler, St. Blasien, Lippspringe, and Reinerz are also especially good. Particularly suitable as winter resorts for these cases are Arco (very mild), Meran (excellent nursing), Gries, Montreux, also the places on the Riviera, notably San Remo, Mentone, Cannes. Hyères, though highly praised, I consider too windy, likewise Bordighera. Nice is for convalescents, but not for invalids (confetti, drinking, Monte Carlo near by). The patient must not expect perpetual sunshine in the south, but must provide clothes and wraps for cold days, the houses being often rather deficient: doors and windows are loose, the floors are of stone, the coverlets are too short, and the stove or chimney smokes. In the large new hotels the conditions have been recently much improved.

The climate of the desert, especially Helouan, Luxor, and Assuan, is only for strong individuals without advanced processes and without fever. The vast distance and the prolonged sojourn arouse an inexpressible longing for home.

Gries and Montreux will do to pass the spring and fall. The choice of such an intermediate resort is very difficult, and depends upon the current weather conditions. In case the early fall is hot, the southern resorts are generally too hot and windy. In case of early autumn storms, the patient should be sent into the mountains. The same holds, *mutatis mutandis*, of spring. There is no doubt that a number of the German summer resorts could be fitted for winter residence.

Patients who have already gained much endurance and strength, and at times, too, those naturally strong with slight symptoms from the beginning, get good results from a sojourn in the *high mountains*.

First comes Davos, the climate of which is excellent, especially in winter; then Les Avants, Leysin, Arosa, St. Moritz, Beatenberg, and Mendel, the latter only for summer.

The advanced stages, hectic, tendency to hemoptysis, anemia, affections of the larynx, albuminuria, empyema, contraindicate high altitudes. Hemoptysis has been recently held to constitute no objection, but further investigations are needed upon this point.

Reinert proposed to use the blood-count as a criterion, on the theory that a considerable diminution of the red corpuscles at lower levels contraindicated the altitudes, "since the hematogenous organs could not respond to the extra demand."

Similarly, the North and the Baltic Sea should be advised only in cases with considerable endurance, preferably after they have shown themselves able to stand the mountains, and by way of clinching what has been already gained. Norderney, especially, ranks well. In cases sent to the sea too early I have repeatedly seen hemorrhages and serious relapses.

Sea trips have been repeatedly recommended (H. Weber), and I myself have seen a number of colleagues who as consumptives became ship's doctors, and returned after one to two years in perfect health. Nevertheless I should be cautious in recommending it. If the sea were sure to be quiet, the rest upon deck, day and night, would be simply ideal for the consumptive. But we must also remember that there are storms and rain, that the patient may be compelled to sleep in a narrow, close cabin, that he may possibly be confined below deck even during the day, that he may suffer greatly from fear, and that he may become the victim of sea-sickness. All the advantages—the pureness of the air, and the improvement of appetite—are then illusory.

I should, therefore, regard a sea trip as an experiment which may just as well injure as benefit the consumptive. At all events we should consider it only for strong or relatively healthy patients. This attitude is justified by the fact that tuberculosis is by no means unknown among seafaring men. Further, even short sea trips, *e. g.*, to Ajaccio, are occasionally associated with so much disturbance that one should always consider it in advising an island climate. For example, two of my patients had stormy weather on the way to Ajaccio, and were kept at sea for forty-eight instead of sixteen hours; one had hemoptysis, the other high fever.

It is different if one has his own yacht, and can run along the coast at will, fleeing into port when the weather is rough.

MEDICAL ATTENDANCE.

Merely transferring the patient to a health resort and a better climate does not mean much for his recovery. Successful treatment of the consumptive depends upon careful observation of a score of details, upon the exact adjustment of therapeutic measures, and upon continuous watchfulness on the part of the physician. Nothing is more foolish than to send a patient away for weeks and months unless he is put in the care of a physician experienced in the case of tuberculosis. The patient often has need of counsel, of encouragement, of intellectual support. The questions of dwelling and of diet are in themselves so important that they demand the advice of a physician acquainted with all the local conditions.

The dwellings in many resorts and even in the institutions are often very unsatisfactory for consumptives. The patient, exhausted by his journey, is glad of a shelter, binds himself to stay a certain time, and recognizes his folly when it can be rectified only at a great sacrifice. If definite arrangements have not been previously made by letter, the patient should be instructed to go to a hotel at once, and then to be guided by the advice of the physician who will attend him. He must not allow himself to be influenced by any other person in the choice of a physician.

It is well that a brief note for the physician should be entrusted to the patient, or, rather, sent in advance, since letters are often surreptitiously opened and sealed up again. If one has formed a definite plan of treatment, it should be imparted to the physician, but not to the patient; since otherwise the local physician may have difficulties in making the necessary changes in it. In case of difference of opinion, it is therefore advisable to hold communications by letter with the physician, and not to injure his authority by including the patient in the conference.

The consumptive should have minute instructions regarding diet, exercise and rest, and the enjoyment of the fresh air, and these must not be fixed for long periods, but should be altered according to the condition of the invalid, as all phthisiotherapists are agreed (Brehmer, Dettweiler, Penzoldt). The consumptive varies daily. If he knows and trusts the physician, he is much more likely to consult him upon apparently unimportant disturbances, *e. g.*, slight fever; otherwise he defers the consultation from day to day, until the critical time has gone by.

Not rarely a consumptive in a health resort comes to the resident doctor, and complains bitterly that he has been in the place four weeks, has faithfully followed the written instructions of his physician, and yet he keeps getting worse. When asked why he did not come sooner, he answers that his physician had expressly said that he could do without a doctor. His condition has changed, meanwhile, and his written instructions are no longer suited to the needs of the case.

When time and money have been spent without avail, the patient is apt to bitterly upbraid his former adviser. What explanation is there for so serious a blunder? It cannot be due to regard for the financial interests of the patient, since one line from the physician would secure free treatment to a poor patient.

To leave the patient to himself is against the fundamental principles of rational phthisiotherapy, and imperils the success of the entire expensive trip.

INSTITUTIONAL TREATMENT.

This offers certain peculiar advantages, namely, a more perfect combination of beneficial conditions with avoidance of the injurious factors. Nevertheless the narrow view which regards institutional treatment as the only cure for consumptives has no foundation in fact. Whosoever has critically and impartially studied the conditions in the various places, whosoever has formed his opinion from a long personal experience and not from books, will agree that both the health resorts and the institutions fall very far behind the claims which are made for them on paper. Here and there the buildings, the nursing, or the discipline will be found to be anything but satisfactory. But this is not the place to enter into details.

The choice between the sanatoria and the resorts at large cannot be categorically decided, but depends upon several circumstances, particularly the individuality of the invalid. The expense of a sanatorium is considerably greater, and, inclusive of the unavoidable accessory expenditures, runs up to 15 to 20 marks a day and even more in Germany. Immature and unformed characters will generally do better in sanatoria, while mature and sensible individuals do as well outside them. For those who are melancholic, the life of a sanatorium, the continuous association with fellow-sufferers, the inexhaustible topics of expectoration, cough, bacilli, fever, and the deaths within the narrow circle, are very unsuitable. A too prolonged sojourn in sanatoria, perhaps over years, is not advisable, since it destroys all independence of life. If conditions remain stationary for any length of time, it is advisable to change—whether it be a sanatorium or simply a health resort. The change serves, also, to relieve the monotony of even good surroundings.

If, however, exception is taken to the sanatoria on the ground that the aggregation of consumptives seriously increases the danger of infection, I cannot agree; assuming, of course, that the superintendent observes the rules of prophylaxis, and that the patients are made to use spittoons or the sputum-cups of Dettweiler. It appears from the data previously given that this danger is minimal, for wards filled with consumptives yielded no bacilli if the proper precautions were observed. The danger is certainly less than in places in which there is no prophylaxis, and to which consumptives come at will. (Upon the promenades there is practically no danger.) Many sanatorians are opposed to even the most essential measures, and persist, for example, in following the old method of sulphur fumigation, which has long been discarded as worthless.

The recent assertion of Flügge that it is not the dried sputum but the droplets disseminated through the air by cough which constitute the chief danger of infection would be fatal to the sanatoria. It has, however, been shown that the theory of Flügge does not correspond to fact (see pages 101, 253, and 501).

The private institutions for pulmonary invalids are: Görbersdorf, 561 m., Dr. Brehmer's sanatorium, founded in the fifties. Dr. Kobert, yearly average 700 to 800 patients. Board (including milk, kefir, baths, douches, massage, etc., and medical attention) 6.50 marks. Room extra; entrance fee, 25 marks. Also cheaper board with moderate prices. Fine, extensive parks.

Railway connections: Dittersbach (Breslau-Freiburg), Friedland (Chotzen-Halbstadt). In addition, there is Dr. Rompler's sanatorium with similar equipment, and Dr. Weickert's in which the price is less.

Falkenstein in the Taunus, 400 m., Dr. Hess; consultant: Dr. Dettweiler. About 400 patients yearly. Rooms, 1 to 7.50 marks a day. Board, without nourishing drinks, 8 marks, including medical advice. Entrance fee, 20 marks. Heating, medicine and instruments, baths, douches, and massage, separate. Via Frankfurt-Cronberg, and thence by carriage (30 minutes), or the Taunus road, or Höchst-Soden and thence by carriage (50 minutes).

Hohenhonnef, 236 m., opened 1892. Dr. Meissen. Rooms, 2 to 8 marks a day. Nourishing drinks, medicine and instruments, massage, baths, and douches, separate. Station Honnef on the Rhine (right bank of the Rhine), Königswinter, Rolandseck (left bank of the Rhine). Comfortably fitted.

Davos, Dr. Turban's sanatorium. Board, including treatment, massage, douches, baths, heat, light, and service, 11 francs. Rooms, 2 to 7 francs a day. Entrance fee, 20 francs. Railroad via Zurich-Landquart-Davos or Bodensee-Landquart-Davos.

Reiboldsgrün, about 700 m., Dr. F. Wolff. Board 38 marks. Rooms, 7 to 25 marks. Entrance fee, etc., extra. Station: Auerbach in Saxony (and Rautenkranz).

St. Blasien, 800 m. Dr. A. Sander (formerly Dr. Haufe). Board, medical advice, and treatment (including rubbing, douches, etc.), 7.50 marks, exclusive of light, heat, and nourishing drinks. Rooms, 1.50 to 6 marks per day. Entrance fee, 10 marks. Post twice daily for Titisee (Freiburg in Br.-Neustadt) and Albbruck (Basel-Constance).

Schömberg in the Württemburg Black Forest, 650 m. Dr. Baudach. Board, including room and treatment, exclusive of wine, 5 to 8 marks a day. Station Liebenzell or Höfen (one and a half hour's trip).

Nordrach-Colonie (Black Forest of Baden). Dr. Walther. Station Biebrach-Hell, Black Forest road.

Blankenhain in Thuringia, 355 m. Dr. Friedmann's sanatorium for throat and chest. Dr. Silberstein. Road, Weimar-Blankenhain.

Altenbrak in the Harz near Blankenburg, 310 m. Dr. Pintschovius. Station Blankenburg and Valley.

Leysin sur Aigle. Canton Waadt, Switzerland, 1450 m. Sanatorium.

Arosa, 1860 m., Dr. Jakobi. Mail twice daily from Chur.

STATE INSTITUTIONS.

The treatment of needy consumptives can be carried out only in a very imperfect manner at home. Moreover, the general hospitals, the usual resort of the poor, are not at present in a condition to treat these cases. The private sanatoria are excluded on account of their prices, and the health resorts at large offer no cheap and satisfactory accommodations. These facts, in connection with the proof that the aggregation of consumptives does not enhance the danger of infection, inspired the establishment of public institutions. England has long had the famous Brompton Hospital (founded in 1841) in London, and the National Hospital for Consumption in Ventnor, etc. Driver, Goldschmidt, the author, Dettweiler, Hermann Weber, Finkelnburg, Penzoldt, v. Schrötter, and especially v. Leyden, first emphasized the necessity of properly caring for these cases, in Germany and Austria. The literature has recently become very extensive, and already many of the German districts have their sanatoria as memorials of a beneficent charity.

Sanatoria of the city of Berlin: Malchow, Blankenfelde, Sütergotz.

People's Sanatoria Association of the Red Cross: Grabowsee.

Berlin-Brandenburg Sanatoria Association: Belzig, in course of construction, for 200 patients.

Next to this sanatorium, the Bleichröder foundation for 30 patients.

Insurance institute for old age and invalidism, Berlin: Beelitz, construction decided on, for men and women.

The association for convalescent homes for patients with lung diseases without means in the government-district Stettin is to begin building in Hoeckendorf.

Uppersilesian sanatorium in Loslau (Gov. dist. Oppeln), for 85 male patients. Opened middle of 1898.

Dr. Weickert's home for patients in Görbersdorf.

Knappschaft-Sanatorium Sülzhayn in the Harz (R. R. station Ellrich). Opened October, 1898. One hundred and ten patients. Connected with it a farm of 73 acres. Opportunity for field work.

Insurance institution for old age and invalidism for Brunswick, Strege in the Harz, named Albrechtsheim, opened June, 1897.

Insurance institution for old age and invalidism for Hanover: Königsberg near Goslar.

Insurance institution for old age and invalidism in Lübeck: Oderberg near St. Andreasberg in the Harz. One hundred and fifteen male patients; opened 1897. Building decided upon for 120 female patients in the neighborhood of St. Andreasberg.

Assisted by the central committee of the Red Cross Felixstift at St. Andreasberg; also for those of less means.

People's sanatorium of the circuit, district Altena i W. near Lüdenscheid. Opened August 1, 1898. One hundred male patients.

Convalescent Association of Frankfurt: Ruppertshain.

Kassel Red Cross sanatorium for pulmonary diseases: Oberkaufungen (100 beds) in construction.

Sanatorium for tuberculous patients without means in Hamburg: Geesthach in course of construction.

Oldenburg Sanatorium Association: Collections and contributions to insurance institution.

Bremenburg Sanatorium Association: Rehburg.

Saxon People's Sanatorium Association: Albertsberg, near Auerbach i. b. Founded end of 1897. One hundred and twenty male patients. Work in conformity with cure (two hours). It has been decided to build a second sanatorium for female patients.

Free forest lodge in Dresden: Sanatorium for Elb sandstone workers in Saxon Switzerland.

The patriotic institute of the women's associations in the Grand Duchy of Saxe with assistance of the insurance institution in Thuringia. Berka a. I. Also for those with small means.

Insurance institution for age and invalidism. Hessen allows 350,000 marks for the erection of a sanatorium for pulmonary diseases at Sandbach in the Odenwald.

The insurance institution for Baden is occupied with the erection of an institution near Marzell for 100 male patients.

In Baden; also Arlen, south of Hohentwiel, in connection with the Heinrich Hospital, founded 1897.

In Stuttgart. Committee appointed and institution for 100 beds planned.

People's sanatorium association for Upper Bavaria: Planegg-Krailing, near

Munich, for 120 men. Opened summer 1898. Sanatorium for female patients with lung disease to follow.

City of Munich: Sanatorium for 200 patients in Harlaching in construction.

People's sanatorium association for middle Franconia: Engelthal, near Hersbruck, near Nürnberg, in construction

People's sanatorium association for the Palatinate: Construction decided on with participation in the sick funds.

Anilinfactory, Ludwigshafen: Dannenfels, sanatorium for workingmen with pulmonary disease, 18 beds. Duration six to eight months. The subsistence of the families cared for.

Austria: Alland near Baden.

Switzerland: Basel Sanatorium, Davos village.

Switzerland: Bern Sanatorium, Heiligenschwendi, 50 beds. Further projects for Zurich, Basle, the French cantons and Glarus.

Russia: Halila, Alexander Sanatorium (Finnland). New great foundation of the Czar.

France: Several institutions for tuberculous children. Sanatorium inAngicourt.

Sweden: Gift of 2,220,000 crowns from the King for the erection of a sanatorium for pulmonary diseases.

[The following is a list of the principal Sanatoria and Hospitals for Consumptives in the United States and Canada.

Arizona:

Mercy Hospital, Sisters of Mercy, Phoenix.
St. Joseph Hospital, Sisters of Mercy, Prescott.
Sisters of St. Francis, Tucson.

California:

Esperanza Sanatorium, Altadena.
Ballard Pulmonary Sanatorium, Pasadena.
Indio, ranch owned by N. O. Nelson, Leclaire, Ill.
Los Angeles, Dr. Barlow's Sanatorium.
Monrovia, Dr. Pottenger's Sanatorium.

Colorado:

National Jewish Hospital for Consumptives, Denver.
The Home, Denver.
The Nordrach Ranch, Colorado Springs.
Colorado Sanatorium, Pueblo.
The Rocky Mountain Industrial Sanatorium, Denver.
Colorado Springs, Glockner Sanatorium.
Y. M. C. A. Health Farm, Denver.
County Farm, Pavilion for Consumptives, Denver.
Agnes Memorial Sanatorium, Denver.

Connecticut:

Dr. Brooks' Sanatorium, New Canaan.
Sanatorium to be opened in the spring of 1904, Wallingford.

Delaware:

State Hospital for the Insane, separate building especially erected for tuberculous insane, recently opened; Farnhurst.

Illinois:

Cook County Hospital for Consumptives, Dunning.

St. Ann Sanatorium for Consumptives, West 48th Street, Chicago.

The Alexian Brothers' Hospital Consumptive ward, Chicago.

St. Elizabeth Hospital, Chicago.

Chicago Sanatorium for Tuberculosis, Chicago.

Indiana:

Fort Wayne, St. Rochus Hospital for Consumptives, West End Main Street. Branch of the City Hospital just completed, Indianapolis.

Iowa:

Boulder Lodge Sanatorium, Fort Dodge.

Louisiana:

Dr. G. R. Tolson's Private Sanatorium, Covington.

Maryland:

Hospital for Consumptives, Towson.

Bay View Asylum, Consumptive department, Baltimore.

Massachusetts:

Almshouse Hospital, separate building for consumptive men, Boston.

Private Sanatorium of Dr. D. P. Butler, Jr., Rutland.

State Hospital for Insane, separate building for consumptive men, Tewkesbury.

Sharon Sanatorium, Sharon. Dr. Bowditch.

House of the Good Samaritan, Boston.

Massachusetts State Hospital, Rutland.

The Millett Sanatorium, East Bridgewater.

Channing Home, Boston.

Free Home for Consumptives, Quincy Street, Boston.

Cullis Home for Consumptives, Boston.

Michigan:

Tent Colony at County Hospital, Detroit.

Minnesota:

Special Hospital for Tuberculous Prisoners, Minneapolis.

Mississippi:

Special Hospital for Tuberculous Insane, Jackson.

Missouri:

Mount St. Rose Sanatorium, St. Louis.

New Hampshire:

Pembroke Sanatorium, Pembroke.

New Jersey:

State Sanatorium, Glen Gardner, Hunterdon County.

New Mexico:

St. Joseph Hospital, Albuquerque.

Chico Springs Sanatorium, Chico Springs.

East Las Vegas, Ladies' Home Sanatorium, East Las Vegas.

St. Anthony's Sanatorium, East Las Vegas.

The Alameda Ranch, Los Cruces.

St. Vincent Sanatorium, Santa Fe.

Sunshine City, Santa Fe.

Pines Cottage, Silver City.

St. Joseph's Sanatorium, Silver City.

Fort Bayard, United States Sanatorium for Soldiers and Sailors.

Fort Stanton, United States Sanatorium for Soldiers and Sailors.

New York:

Adirondack Cottage Sanatorium, Saranac Lake.

Prescott Reception Cottage, Saranac Lake.

Sanatorium Gabriels, Paul Smith's.

House of Rest for Consumptives, Bolton Road and 209th Street, New York City.

Home for Consumptives, Brooklyn.

The Liberty Sanatorium, Liberty.

Edgemont, Liberty.

Dr. Stubbert's Tent Colony, Liberty.

The Loomis Sanatorium, Liberty.

Manhattan State Hospital, East Ward's Island.

Montefiore Home Country Sanatorium, Bedford Station.

St. Joseph's Hospital for Consumptives, New York City.

Seton Hospital, Spuyten Duyvil.

Tuberculosis Infirmary, Blackwell's Island.

Riverside Sanatorium, North Brother Island.

Stony Wold Sanatorium, Lake Kushaqua, Franklin Co.

Raybrook, Franklin County State Hospital for Incipient Cases of Tuberculosis, opened February 1, 1904.

Hill Crest, Santa Clara, Franklin County.

Dannemora, Clinton Prison, separate building for tuberculous prisoners.

East View, County Hospital, Yonkers.

North Carolina:

Asheville Sanatorium, Asheville. Dr. W. S. Battle.

Southern Pines Sanatorium, Southern Pines. Dr. Edwin Gladmon.

Pineshire Sanatorium, Southern Pines.

Winyah Sanatorium, Asheville.

St. Joseph's Retreat, Asheville.

North Dakota:

Oak Park for Consumptives, Minot.

Ohio:

Municipal Tuberculosis Sanatorium, Cleveland.

Cincinnati Branch Hospital for Consumptives, Cincinnati.

Pennsylvania:

Free Hospital for Poor Consumptives, White Haven.

Home for Consumptives, Philadelphia.

Scranton Sanatorium, Scranton.

Nott Home of Jewish Hospital, Philadelphia.

South Mountain Camp Sanatorium. Dr. Rothrock, Mt. Alto, Franklin County.

Bide-Awhile Sanatorium, Perkiomenville.

Henry Phipps Institute maintains hospital of 52 beds for incurable cases, Philadelphia.

House of Mercy, 411 Spruce Street, Philadelphia.

Lakewood Sanatorium, 1932 N. Main Street, Scranton.

West Mountain Sanatorium, Scranton.

Sunny Rest, private, White Haven.

Rhode Island:

Burrillville State Sanatorium, Burrillville.

Pine Ridge Camp, Foster.

South Carolina:

Aiken Cottage Sanatorium, Aiken.

Texas:

Agricultural Colony for Tuberculous Prisoners.

Hotel Dieu, Sisters of Charity, El Paso.

Camp Reliance, Comfort.

Dr. W. L. Cook's Sanatorium, Boerne.

Vermont:

The Champlain Open-air Sanatorium, South Hero.

Washington:

Tent Colony at King County Hospital, Seattle.

Canada:

Free Home for Consumptives, Gravenhurst, Ontario.
Muskoka Cottage Sanatorium, Gravenhurst, Ontario.
Montreal Sanatorium for Consumptives, Montreal, Quebec.
St. Agatha, Quebec, Provincial Sanatorium.
Provincial Sanatorium projected, Manitoba.
Provincial Sanatorium projected, Nova Scotia.—Ed.]

Private foundations of this sort must rejoice every humanitarian. It is also part of our socio-political theory to do everything necessary and possible for the recovery of our infirm members. Therefore the care offered by the Age and Infirmity Insurance Societies has not only its selfish but also its humanitarian aspect. For there is no doubt that properly selected cases will entirely recover in the public institutions, and still others will be kept alive for a number of years and made capable of bread-winning, whereas they would otherwise have succumbed to the unequal battle and would have been a burden upon the insurance societies.

As one of the first who championed these establishments by word and deed, I cannot refrain from issuing a warning against the too roseate hopes which they have often aroused, lest the disillusionment be overwhelming. According to my experience, the three-months' cure is too brief; it may bring about improvement, but rarely, even in milder cases, a definite cure. The patients are discharged relatively cured, return to their old surroundings, to their hard labor in dusty work-shops, most of them being workmen, and to their unhealthful dwellings, and it is not strange that the process begins anew. I know of cases in which hemoptysis occurred fourteen days after the patient had been discharged as cured. Such events make us cautious in our opinion of the cures.

The literature of the subject is often careless in its statistics. One author calculates that 13 per cent. of recoveries means a saving of more than 100,000 lives; another widely read author is satisfied with 80,000. Such data are without foundation, and as the future proves them false, they can only injure the cause.

The discontinuance of the treatment ordinarily depends less upon the desires of the patient or his homesickness than on the financial difficulty connected with the support of himself and his family. Difficult as it is to raise the money for the convalescent patient, it is far more so for the family, who usually forfeit the sick-money after the thirteenth week and are then without funds. And even after recovery the cicatrix in the lung constitutes a *locus minoris* *resistentiæ*, which is predisposed to reinfection when the patient subjects himself to the old environment with its dangers.

The establishment of these institutions is only a half-measure, the enormous outlay of money useless, the success only apparent, if we do not also give heed to the immediate future of the patient, if we do not improve the conditions of the home, do not relieve him of a part of his responsibility toward his family, and supply him for some time with a less injurious occupation and keep him busy, if possible in the open air—requirements which it is easier to enumerate than to fulfil.*

Praiseworthy as are these public establishments, I doubt whether by their means singly or chiefly any marked decrease in tuberculosis can be achieved within a limited period of time. If we consider the extent of the disease, this would require sums which are practically unobtainable.

The establishment of such institutions is and remains an unsatisfactory measure, if it is not associated with prophylaxis, which is not only far less expensive, but has already stood the test of experience and has diminished tuberculosis by almost a third (see page 519); if, furthermore, the scope of the latter is not very considerably increased.

Unfortunately, prophylaxis for communities is barely touched upon in the literature, and yet we certainly confer a far greater benefit on the laborer if we see to the preservation of his health than if we interfere only after the disease has already taken a foothold and the chances of recovery are questionable. The humanitarian instincts and social and political interests are all far better served by averting the disease than by treating and curing it. Only after a careful and serious prophylaxis has still further reduced the extent of the disease will the public sanatoria be in a position to accomplish their part of the task.

It is a serious gap in the undertaking that the laboring class is alone the gainer, while the great middle class—teachers, small tradesmen, and artisans, who are financially just as helpless against the disease—are hardly considered.

As yet, the chief advantage of these institutions lies in the fact that the knowledge of hygienic and dietetic principles there imbibed is, to a certain extent, disseminated abroad and thus given a wider sphere of influence. Recently I made an investigation into these institutions, and repeatedly observed that the beautiful reclining rooms and the easy-chairs were deserted, and that the patients were up in their rooms—playing cards.

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* I refer to the excellent and practical works of Weickert.

The establishment of these institutions, moreover, does not exonerate us from the duty of reforming our hospitals, in such wise as to give recognition to the more important, at least, of the principles of phthisiotherapy. Separation from other patients, pavilions, reclining rooms, are requirements which have not yet been satisfied. Specialization in the treatment of consumption widens and deepens our knowledge of this disease, which above all others saps the strength of the race.

LENGTH OF SOJOURN IN THE RESORTS.

The stay of the patient in the resort or sanatorium ought to be prolonged until his cure is accomplished. But only in rare cases can the patients be spared from their families and their business for this length of time. Where, from material considerations, time is limited, the physician should select the most favorable chance. Prejudice and the old tradition that cold is injurious lead most physicians to send their patients away in winter. Local conditions should, however, constitute the sole criterion. If the summers are beautiful and free from dust, and the winters raw in the place where the patient lives, he should be sent away for the winter. If the winter is mild, and the summer dry and dusty, he should stay at home in the winter and go away in the summer.

It stands to reason that a disease of this character, which is chronic and of many years' duration, which is inaccessible to direct interference, and in which the efforts of the physician are necessarily limited to providing favorable surroundings and excluding injurious influences, cannot be cured within six to eight weeks. After months of treatment, indeed, cough, expectoration, and sweating may diminish or disappear, but the disappearance of the symptoms does not denote recovery.

Four to six weeks comprises the natural period of treatment at the springs, and this seems to have suggested the same brief limit for consumption. In the latter disease, however, a sojourn of about three months, as generally practised in the sanatoria for the poor, is too short to give permanent results.

Wherever possible, one should advise a sojourn of three or four months, one-half year, one year, or more, in proportion to the severity of the condition and the means of the patient. If the tuberculosis has progressed considerably, it is proper to warn the patient that for one to three years he must devote himself to the care of his health.

With those of less means the physician must exercise great care not to awaken the unspeakably sad and bitter feeling that only their poverty stands in the way of recovery. Patients much attached to home and family should not be frightened by suggesting too long a time. Under other circumstances, the physician spares himself and the patient many annoyances and troubles, if he makes clear to him the necessity for a prolonged absence, and does not entice him from home on the promise of a brief six weeks of treatment. For the business man must make arrangements for his prolonged absence; another must engage a substitute; officials must get long leave, etc.

SPECIFIC TREATMENT.

The hygienic and dietetic treatment may claim good results, especially in the initial stages, but demands a great expenditure of time and money, and yet is apt to fail in the advanced stages. Hence the search for simple, cheap, and certain specifics. To describe even approximately all that has been advised for the treatment of phthisis would fill volumes. I shall, therefore, restrict myself to the chief remedies and to certain methods of combating the disease. An excellent résumé of the works which have appeared from the time of the discovery of the tubercle bacillus till 1888 is to be found in Wesener.

CHEMICAL REMEDIES.

Tannin is one of the oldest specifics. It was used in the eighteenth century, and highly valued but gradually forgotten. Woillez resuscitated it in 1863, and Raymond-Arthaud, having tested it in animals, employed it in men; they claim improvement and arrest of the process, likewise de Jager and de Viti-Demarco. My experiments on animals yielded no results. It is prescribed thus:

℞.	Ac. Tannici	5.0
	Glycerini	30.0
	Vini	ad 1000.0

Sig.—One wineglassful after meals.

Or—

℞.	Ac. Tannici	2.0–4.0
	Aq. Dest.	100.0
	Albi Ovis	1.0

M. Sig.—Take during the day.

Plumbum aceticum has been and is still largely credited with a favorable influence upon the tuberculous process. My own observations do not confirm this theory.

Garlic. Galician physicians assert that tuberculosis is rare in places in which garlic is used in large quantities. I could determine no effect from rectal injections.

Sulphuretted hydrogen and carbon dioxid. Claude Bernard's discovery that sulphuretted hydrogen injected into the rectum is excreted by the lungs suggested to Bergeon his famous method of treatment by rectal injection of this gas and of carbonic acid. He claimed that it considerably improved the general condition, but admitted that the bacilli in the sputum were not diminished. Of the many subsequent observers, some confirmed his views, others directly disadvised the method (Bardet, Burney, Babcock, Statz, Pavay, Farnos, Cornil, and Dujardin-Beaumetz). Bergeon himself had to admit that his method did not cure. It is no longer employed.

Corrosive sublimate, so excellent a disinfectant outside of the body, is utterly ineffective against tuberculosis, according to the conclusions of Koch, Gosselin, Laplace, and the author. Continuous injections did not disturb the growth of the bacilli. The other mercury compounds are similarly inactive.

Creolin is of varying composition; according to my experiments, but contrary to those of others, it is inactive against the tubercle bacillus, but not innocuous to the body.

Iodoform. According to Semmola, iodoform, the favorable effect of which in surgical tuberculosis is well recognized (0.05 to 0.5 each day, with extr. gentianæ or other extract internally, or in turpentine for inhalation), diminishes cough, fever, and expectoration, and improves the general condition. Dreschfeld also had satisfactory results. Schnitzler saw no actual cure, but also no untoward results. Other authors obtained no results.

Arsenic, used in earlier times against phthisis, was reintroduced by Buchner. It was supposed to stimulate the living tissues in their struggle against the bacteria. He used the arsenious acid in watery solution, ran the dose up to 10 mgs. a day, and claimed to have observed marked quiescence of the process. Stintzing, Guttmann, Fräntzel, Lublinski, von Leyden, the author, and others do not confirm this. There was at most an improvement in the nutrition, such as was already known, but otherwise no specific influence upon the process.

Phosphorus and the hypophosphites, the former recommended by Buchner, have not found a place in the therapy. The same is true of terpin, first tried by Lépine, and recommended by Sée for the cough and expectoration of the catarrhal form of the disease. It has not been credited with specific action. Brugnatelli confirmed these findings, Kien failed to see any good results.

Verbascum thapsus. The leaves cooked in milk were warmly recommended by Quinlan as an ancient and popular remedy against consumption in Ireland; he reports recoveries and cures. Richardson and Bampton found it useless.

Phellandrium, according to Almès, retards the progress of the disease.

Carbolic acid was used by Filleau internally (2 : 400 of glycerin), and subcutaneously (1 per cent. solution 5 gm. each time; according to a later publication, 2 per cent. solution). With Léon-Pétit he describes good results. Ley, too, saw the bacilli disappear from the sputum after the injections, and Hartigan found considerable improvement after inhalation.

Roussel injected **eucalyptol,** and saw rapid improvement and diminution or disappearance of the bacilli from the sputum. His reiterated praises of the drug have not been fully echoed by others and have been in part discredited—Ball, Bouveret and Péchadre, Ley, Habert, and Pons. Robson claims that saturation of the air of the room has brought about apparently permanent cure.

Boric acid. Canio ameliorated the symptoms by inhalations of pulverized borax; likewise Schoull, combining it with creosote, iodoform, and arsenic.

Hydrofluorides. Used even before the time of Koch, they were highly praised by Chevy, Seiler, and Garcin. Hérard considers them of value. They have found many adherents in France, but the majority claim only amelioration of the symptoms but not cure (Lépine and Paliard, Moreau and Cochez, etc.). Jaccoud denied that the dilute acids had any deleterious effect upon the bacilli.

Anilin was recommended by Kremjanski. His claims were overthrown by the investigations of a self-appointed commission after Fräntzel had given warning of the danger of anilin. Bertalero and Albitski, nevertheless, claim to have had good results.

Resorcin. Leblond claims to have cured 22 out of 31 consumptives by the inhalation of the fumes of resorcin.

Camphor (in carbolated oil) injected first subcutaneously, then into the lungs, led to considerable improvement, according to Smith. Huchard, Faure, and Miller observed a return of sleep and appetite, and cessation of sweats, and general improvement; after eight days the injections are suspended for two days. Alexander, especially, has recommended the subcutaneous injection of camphor oil (in case of fever, 0.1 to 0.2 for six weeks, then four weeks' pause, in cases without fever, 1.0 for four days, then eight days' pause).

Menthol was first used by A. Rosenberg, and then by Beehag, in laryngeal and pulmonary tuberculosis, with good results. S. Rosenberg and Fürbringer are less satisfied with the result. In my experiments on animals I could not find that the tuberculous process was materially affected; the lung smelt, indeed, very strongly of menthol, but was full of well-developed bacilli. Decomposition alone was interfered with. It is possible that menthol might be of service in mixed infections.

Creosote was discovered by Reichenbach in the year 1830, and employed against tuberculosis. At first made much of, especially in England and Germany, it was gradually forgotten. In 1877 Bouchard and Gimbert again turned their attention to it, and in 1883 Pick, in 1887 Fräntzel, and especially Sommerbrodt, the latter with an experience of nine years and 5000 cases, have warmly recommended the drug.

Sommerbrodt administered creosote in capsules of creosote 0.05 and balsam of tolu 0.2; he began with one capsule and increased to nine. In a later communication he advises as much as 4 gm. a day. These favorable criticisms have been confirmed by Kaatzer, Sée, von Brunn, Guttmann, Sticker, Kernig, Poslawski, and many others. Even though creosote, in my experiments on animals, was unable to hinder or delay the growth of the bacilli in the body, and could not inhibit the process of destruction, it is still possible that the drug has some favorable effect upon the body. Especially in cases in which the expectoration is very abundant and full of bacilli, creosote diminishes the amount and retards or even arrests the process. The essential factor is probably the improvement of the digestion (Klemperer), of the appetite and the nutrition, which is at times seen to follow its use. There are, indeed, cases in which creosote produces the contrary effects—anorexia, vomiting, indigestion, and diarrhea, which immediately contraindicate its use. Irritation of the kidneys (watch the urine) occasionally occurs with prolonged use or large doses, therefore nephritis is a contraindication. Hemorrhages are likewise to be considered.

It may be administered either in the old way with wine—

℞.	Creosote	15.0
	Tinct. Gent.	30.0
	Spir. Vin. Rect.	250.0

M. Sig.—One teaspoonful several times a day.

or in water or in gelatin capsules (0.05 or 0.1 with balsam of tolu or cod-liver oil).

Sometimes patients like to take it in drops (one of creosote, two of Tinct. Gent.) in meat powder or bread powder. The officinal pills I rarely order, since I have convinced myself of their elimination in the stools unchanged. The best average daily dose is 1.5 (Gimbert and Schetelig). In view of the effect on the kidneys, it is not well to give large doses (4.0) too long.

Creosote has also been given subcutaneously by some authors (20 to 30 per cent. of the above solution).

The unpleasant, even corrosive, action of creosote and its variable composition, have led to the use of its chief ingredient, guaiacol (Sahli, Penzoldt), which is used in the same way. Combinations of the latter with acids are also used, *e. g.*, guaiacol benzoicum (benzolol, 2.0 to 5.0 pro die). It is generally well taken, and improves weight and appetite.

Within the last few years pure creosote and guaiacol have been largely replaced by their carbonates, creosote carbonate (creosotal), and guaiacol carbonate (duotal)—the former a thick fluid of slightly bitter taste, which is decomposed in the gut into its components; the latter a white, odorless, tasteless powder. Both drugs, about equal in their effects, are greatly superior to creosote or guaiacol, in that they are far better borne by the stomach, produce neither vomiting nor irritation, and at the same time effect an improvement in the appetite and the strength, and a diminution of the secretions—in a word, a change for the better. Only recently Jakob and Nordt reported some very good results from von Leyden's clinic, and my own experience confirms these findings.

Creosotal is given to the patients three times daily, in milk, red wine, capsules, or bouillon (one quarter of an hour after meals); one begins with five drops, increasing by two to five drops up to about 30 drops, for six to eight weeks. Then one intermits for about eight days and starts afresh. Very large doses, as recommended by Chaumier, not rarely produce aversion and indigestion.

Duotal is often borne better in doses of 0.2 to 0.5 three times daily, increased slowly to 1 to 2 gm., in wafers or as such followed by water (in children, 0.1 increased to 0.5, thrice daily).

Recently, Grawitz and Zinn have recommended *creosote valerianate* (eosote) as a drug which is well borne even in large doses, and as having the effect of creosote without its disagreeable action on the stomach and intestines: administered in capsules of 0.2 gm. one, two, or even three capsules thrice daily. The same holds true, as regards action and dose, of geosote, the valerianic acid ester of guaiacol (Rieck).

Ichthyol. This was first (1894) brought into notice by M. Cohn and G. Scarpa, simultaneously. The former claims that it has an anti-bacterial action, that it prevents the destruction of albumin, and, even in large doses, has no disagreeable associated effects. He gives 2 to 50 drops of ichthyol and water, in plenty of water three times daily before meals, and follows it with black coffee or lemonade. Ichthyol has no specific action, but occasionally increases strength. The taste and the frequent belching are unpleasant. Unna has used it successfully for many years to improve the general condition in all consumptives. Le Tanneur, too, reports good results both as regards the general condition, and also the cough, the expectoration, the dyspnea, the intercostal pain, the sweats, and the appetite; he gives it in capsules of 0.25, four to twenty-four daily, *i. e.*, about 1 to 6 gm. daily.

Potassium cantharidate has been given by Liebreich in doses of 0.0001 to 0.0002 subcutaneously, both for tuberculosis and other inflammations. He had found that it called forth an exudation of serum from the capillaries, especially in diseased areas, and believed that this serum was bactericidal. The experience of most investigators (Guttmann, Herzfeld, etc.) has not borne out his expectations. The slight effect and the frequent injury to the kidneys hardly encourage us to further trials.

Cinnamic acid. Landerer conceived the idea of turning tuberculous foci into solid cicatrices by means of inflammation. Having in mind the erysipelas inoculations in cancer, and, at the same time, the difficulty of controlling the bacteria, he attempted to set up aseptic inflammation by chemical means. For this purpose he first made injections of an emulsion of Peru balsam; he was led to this by the theory, subsequently partially confirmed by microscopic investigation, that the finest particles are deposited in greatest number in the tuberculous focus. In order to attain a higher concentration, he then made use of what he considered the most active ingredient of Peru balsam, namely, cinnamic acid, which he first made into an emulsion, and later, for the sake of ease in the preparation, into a watery solution of the cinnamic salt.

In rabbits and men treated with this preparation, Landerer believed that the tuberculous focus first showed a dilatation of the capillaries, then a large exudation of leucocytes, then the formation of epithelioid cells, encapsulation and fibroid organization, and finally absorption of the necrotic masses and cicatrization.

At present Landerer uses cinnamic acid from the factory of Kalle (Biebrich a. R.), chiefly the sodium salt, called *hetol*, in a 5 to 10 per cent. slightly alkaline solution in hot water, or, better, in physiological salt solution. The solution is to be filtered and sterilized, and kept in colored bottles. Injections should be made into the thin-walled veins of the elbow or into the lower part of the cephalic vein, the technic being practised, if necessary, on a rabbit. The venous circulation of the arm is first arrested by means of a moderately light rubber bandage, the selected area cleansed with sulphuric ether and 0.5 per cent. sublimate, and the arm put into proper position, preferably in extension at the elbow. The syringe should be reserved for this use, should be sterilized in a 1 per cent. soda solution, and then carefully washed out with sterile salt solution; the cannula should be laid in 80 per cent. rectified spirits for one-half hour, and the air carefully expelled. The gluteal injection (dose one-half to one-third more) into the upper part of the buttock, avoiding the sciatic nerve and the sciatic foramina, is used by Landerer almost exclusively for young children. He finds it, clinically and experimentally, of far less value, and in severe cases entirely useless.

After two to five days of careful observation and temperature measurements, the patient is given the minute dose of 1 mg. of hetol (in cases much run down or with high fever even smaller doses, in initial, afebrile cases higher doses, but never more than 2 mg.) which is gradually increased to the indicated amount. The injections are made every two or three days (decline of the leucocytosis requires twenty-four to forty-eight hours), preferably in the forenoon. The dose is increased by 1, rarely 2 mg., while in very advanced cases it is increased by only 0.5 mg. a week. The maximal dose is 25 mg., very rarely 50, which is best given at the fifteenth injection on the thirtieth day, and beyond this one does not go. After two months more one decreases the dose from 25 to 5 mg., and from 5 to 1 mg., and increases it again somewhat more rapidly. After four to six months there is an intermission of one to two months. If the dose is too large, there is rise of temperature (1°), discomfort, and loss of weight; in severe cases, with a slight rise of temperature of 0.5°, the small doses may be cautiously continued. If the leucocyte count amounts to 1:300 constantly, even after the injections are suspended, an intermission is indicated. In case of weak heart, or of a sense of constriction and distention, also in emphysema, the doses are to be carefully calculated. Especial care is indicated in case there is a tendency to hemoptysis; the dose should be kept below 5 mg. for about six weeks, should be slowly increased, and occasionally discontinued.

In early cases Landerer considers three months sufficient. The effects which he claims are: subjective improvement, disappearance of the night-sweats, diminution of the cough and expectoration, increase of weight, and from about the fourth week on decrease in the number of bacilli; further, the râles become fewer, after a temporary increase, the dulness clears up, but becomes intensified at the apex in evidence of cicatrization; simple tuberculous fever is removed in one to eight weeks, while septic fever is not influenced or is increased.

Landerer asserts that inflammatory pneumonic processes are produced in the proximity of the tuberculous foci by the cinnamic acid, which are to be regarded either as true inflammations or as regenerative processes. As long as the foci containing bacilli are not closed off, excessive doses may stir them up, with mobilization of the bacilli, dissemination of the tuberculosis, and possible death. The drug has not as yet been carefully investigated by others.

All of these methods are based upon the desire to produce a reaction in the neighborhood of the tuberculous focus, and so to wall it off if possible. Assuming their effectiveness, they all labor under a common difficulty, which is, perhaps, shared by tuberculin; in cases at all advanced, the various foci react very unequally, so that a stimulus which just suffices to produce the optimum of reaction for one focus is too large for another and leads to transudation and permeation of the focus, and so favors the dissemination of the bacilli. Experiments on animals in which the foci are about equal in age and reaction, or at least not so diverse, are therefore not to be unreservedly applied to man. This explains the fact that the successes relate mostly to the early stages, in which there is only a single focus—aside from the fact that the chances of cure are then most favorable.

Mineral Water Cures.—These are helpless against the tuberculous process as such. They constitute a valuable aid in decreasing or arresting the accompanying catarrhs of the respiratory organs, the laryngitis, pharyngitis, and bronchitis; they liquefy viscid secretions, facilitate expectoration, and so are indirectly of assistance by hastening the removal of the infectious sputum.

Of service are the sodium chloride springs, *e. g.*, in Reichenhall, Salzungen, and Soden, also the Elizabeth spring in Homburg; the earthy springs, especially the Arminius spring in Lippspringe; the alkaline and alkaline muriatic springs of Ems, Gleichenberg, Salzbrunn, also the Neuenahr Sprudel (in tendency to hemorrhage waters surcharged with CO are to be avoided); the sulphur springs of Weilbach among others; iron waters, *e. g.*, the Schwalbach Weinbrunnen; and arsenical waters, *e. g.*, Roncegno.

BACTERIAL PRODUCTS.

Bacterium Termo.—Very soon after Koch's great discovery Cantani, reasoning on the theory that even among the lowest organisms the survival of the fittest must hold good, experimented with inhalations of Bacterium termo (of the harmlessness of which he had previously assured himself), and believed that he had achieved a brilliant success. Fuckel, Salama, and Karassik confirmed his results, but Ballagi, in eight patients of Brehmer's clinic, whom I meanwhile had the opportunity to observe, could discover neither objective nor subjective improvement. Stachiewicz also reached negative results. The results of other investigators, also, were not very encouraging or absolutely negative—Laaser, de Renzi, Sormani, Testi and Marzi, and others; Lambart alone claimed to have had excellent results. To-day the method is practically abandoned.

Tuberculin.—At the Tenth International Congress, Koch proclaimed that he had discovered substances which immunized guinea-pigs against injections with the tuberculous virus, and which could arrest the process in such as were already in an advanced stage of general tuberculosis. Three months later appeared further contributions upon this preparation, subsequently known as tuberculin, which might be summarized in the statement, based upon clinical observation, that tuberculosis could be cured with certainty in the initial stages by this preparation.

The beginning of his investigation was the observation that the result of inoculation was not the same in healthy guinea-pigs as in those which had previously had tuberculosis. In healthy animals the wound produced by the injection of a pure culture of tubercle bacilli appears to heal up within a few days; but in about fourteen days a nodule forms which breaks down and remains open until the death of the animal. In tuberculous guinea-pigs the small inoculation wound is at first cemented together in the same way; no nodule, however, is formed, but the skin over a fairly wide area is thrown off as a hard and necrotic slough; the resulting ulcer heals rapidly, and the neighboring lymph-glands are not involved. Furthermore, injections of dead cultures of tubercle bacilli in healthy animals produce only local suppuration, while even in small amounts they quickly kill those which are tuberculous; repeated injections of very dilute emulsions, however, arrest the disease, if it is not too far advanced.

Tuberculin is prepared as follows, after the formula of Koch: Cultures six to eight weeks old, which have been grown upon slightly alkaline veal-bouillon or on 1 per cent. solution of meat extract with the addition of 1 per cent. peptone and 4 to 5 per cent. glycerin, are subjected to steam and passed through a clay or silicate filter, being diluted with the nutritive medium to the tenth part of their volume. The result is a thick extract, containing 40 to 50 per cent. of glycerin.

The strength is tested on a guinea-pig inoculated four to five weeks previously, which is killed within six to thirty hours by a dose of 0.5 gm. The liver and spleen, in addition to tuberculous changes, show ecchymotic spots, from the size of a pin's head to that of a hempseed, which are found to be capillary dilatations in the neighborhood of tuberculous foci.

In non-tuberculous men an injection of 0.25 cc. induces a severe reaction, which is far more intense in proportion to the body-weight than in guinea-pigs; 0.01 produces no reaction. In tuberculous individuals the reaction occurs with 0.001, and declares itself within four to five hours by general symptoms—rise of temperature over 39° to 41°, generally after a preliminary chill, pain in the limbs, weariness, cough, often nausea and vomiting, occasionally cerebral symptoms—which last about twelve to fifteen hours. There are also local reactions: external foci show local reddening, swelling, and exudation, which subsequently hardens into crusts and scabs, and falls off; pulmonary foci give râles, increase of dulness, increase of cough and expectoration, and at times the presence of bacilli in the sputum, where these had previously been absent. After one, sometimes two to four days, the reaction subsides, and can be re-induced in equal intensity generally only by increased doses. One begins with 0.001 gm. and increases the dose to 0.01, avoiding any violent reaction by very gradual increase. The injections are generally made in the back with Koch's sterilized syringe. The necessary dilutions of the tuberculin are made not with water, but for the sake of permanence with 0.5 per cent. carbolic acid solution.

During the early period of its use the terminal dose was overstepped, as much as 1.0 being given. The stormy reactions were made light of, and regarded not as contraindications to larger doses, but as symptoms of cure. Upon the basis of Koch's assertion that guinea-pigs could be cured or immunized by rapidly increasing doses, the same attempt was made upon human beings. At that time I submitted 420 consumptives to this procedure, using the high doses also, and in a number of cases, some of which were well advanced, I observed marked improvement and recovery, which has persisted up to the present time (1898).

Example: In the case of a Hungarian official, with extensive processes and fever of 39.5° C., who came to me with his doctor, I hesitated at first to employ the tuberculin treatment, but upon the urgent entreaties of himself and his mother, and in view of the hopelessness of any other form of treatment, I was persuaded to it. The man is healthy to-day, after eight years, is married, and has two healthy children. I could relate a series of similar cases.

Such startling results encouraged further trials, to which other patients were not always suited. It undoubtedly made some cases worse, and in a few (five) of mine it hastened the end. Warning voices made themselves heard, and eventually, in order to avoid all reaction, we came to give very minute initial doses (0.0001) and to rise gradually to 0.02 to 0.05. Some claim good results with this method; others deny it all value, and hold it absolutely harmful.

According to my own experience, the smaller doses never cause anything like the astonishing improvement which occasionally follows the use of the larger, so that it is difficult to determine how much of the result is to be attributed to the tuberculin and how much to the associated hygienic and dietetic procedures; on the other hand, the large doses can no longer be regarded as admissible, in view of the occasional accidents. In cases in which the hygienic and dietetic measures, duotal, creosotal, etc., are unavailing, tuberculin should be given a trial even now, unless the disease is very far advanced or there is a secondary infection. Tuberculin undoubtedly contains a curative body, but its correct use, its preparation is not yet possible.

In 1897 Koch described a new form of tuberculin, known as T. R. It is intended to render the bacilli absorbable.

Fresh, well-dried cultures are mechanically crushed, and the resulting material thoroughly mixed with distilled water and centrifuged. [See Koch's original article.] This form of tuberculin, described as T. R., is credited by Koch with marked immunizing properties. The fluid, preserved in 20 per cent. glycerin, contains 10 mg. of solids in 1 cc.

One begins with dilutions of $\frac{1}{500}$ mg., the injection of which hardly ever produces any reaction. Reactions are to be scrupulously avoided; the course is, therefore, made so gradual that rises of temperature rarely occur. Men first show the undeniable effects after 0.5 to 1 mg. For patients who have a prospect of living only a few months, and for cases with secondary infection, the preparation is unsuitable. The unequal composition of the preparation has been a general source of complaint, and the old tuberculin is preferred.

[Further experience with T. R. has proved that it has no advantages over the old tuberculin, while it is less uniform in strength, and therefore less satisfactory for use.

The term T. O. was applied to the supernatant fluid standing above the T. R. after centrifuging. It is a solution of the soluble toxins contained in the bacillus. Its physiological effects are the same as those of the old tuberculin, over which it possesses no advantages, and its use has been given up.

More recently Koch has introduced "*Bacillen-Emulsion,*" which is obtained by pulverizing the living bacilli and suspending them in 20 per cent. glycerin. It contains all the constituents of the bacillus, and is the most potent of all the products yet obtained from it, and is used in the smallest doses. It has been used to some extent in treatment, but its manufacture is difficult and must be carried out with scrupulous care, while its use has been proved to be not entirely devoid of danger. Its use should be begun with doses not larger than $\frac{1}{20}$ mg. It requires from six weeks to three months to reach a dose of 2 mg. Its utility may still be regarded as *sub judice.* In animals it produces a slight degree of immunity, but considerably less than that brought about by living attenuated bacilli.—Ed.]

Antiphthisin.—Tuberculin was thoroughly investigated by Klebs. He came to the conclusion that it contained two different substances, the one tuberculocidal and of value, the other injurious, the cause of necrosis, inflammation, and excessive exudation of leucocytes in the tuberculous focus, therefore also a cause of fever, cardiac and cerebral disturbances, and possibly of dissemination of the bacilli. The harmful constituents are stored in the bodies of the bacilli; the specific healing substances are contained in the cultural fluid as secretory products. By precipitation of the former with alcohol and bismuth, he obtained from the crude tuberculin of Koch a purified preparation—*tuberculocidin*. More recently, by treating the tubercle-free fluid with sodium-bismuth-iodide in acetic acid and alcohol, he precipitates a substance—*antiphthisin*—the advantage of which is that the somatic toxins of the tubercle bacilli are preliminarily excluded and the active substances not carried over in the form of insoluble albumins, since steaming is not resorted to as in the preparation of Koch's tuberculin. Antiphthisin is provided in two-, five-, and ten-fold concentration of the active substance by the Höchster factory.

Having first convinced himself of the harmlessness and effectiveness of the preparation by trials upon animals, he used it in human beings. According to his directions, one injects antiphthisin daily, and regularly increases the dose, unless fever seems to render it desirable to maintain the same dose for some length of time. Any rise of temperature through its use must be studiously avoided. One commences with the double concentration and injects $\frac{1}{4}$, $\frac{1}{2}$, 1, $1\frac{1}{2}$, 2, etc., up to 4 cc. into the rectum on successive days, then the five-fold concentration (2, 3, 4, 5 cc.), and finally the ten-fold. Klebs claims good results with his method; its harmlessness is also admitted by other authors.

Maragliano's Serum.—Maragliano isolated two groups of bacterial substances from virulent cultures, one by means of concentration of the culture in the water-bath at 100° C., the other by filtration (Chamberland) and compression in a vacuum at room-temperature, and injected these into dogs, donkeys, and horses for six months, raising the dose from 2 to 40 or 50 mg. per kilo. The serum of these animals, according to Maragliano, protects a healthy guinea-pig in a dose of 1 cc. to 1 kilo from an otherwise fatal dose of proteins. In men it is used subcutaneously.

In afebrile cases 1 cc. is injected every other day for about ten days, then 2 cc. per day for another ten days, etc. With fever up to 38° and 38.5° C., the same; in case of higher temperatures, higher doses, 10 cc. at one sitting. If the fever diminishes within three days, daily injections of 1 or 2 gm. are made, otherwise after eight days another 10 gm. Maragliano reports local and general improvement without unpleasant by-effects; a number of Italian physicians (Gay, Ermano, Giura, Nascimbene, Pucci, Bertola, de Renzi, and others) at the Italian Congress of Internal Medicine, and also later, reported similar successes, although in most instances in only a few cases. Further data must be collected. [Further experience with Maragliano's serum has failed to prove its value.—Ed.]

The attempts of other investigators to induce recovery or immunization with serum (Hericourt and Richet, Grancher, Pinard and Kirmisson, Tommasoli, Bernheim, Pagnin) have as yet led to no practical results.

[Many efforts have been made to establish an artificial immunity against tuberculosis, but with absolute lack of success until 1889, when Dasenberg,* and soon after (in 1890) Grancher, Dor, Martin, and Courmont,† attenuated cultures of the bacillus by heat and antiseptics, and then claimed to produce some degree of immunity to the disease by injecting them repeatedly into rabbits.

In May, 1893, Trudeau‡ succeeded in bringing about a relative immunity in rabbits by repeated inoculation of cultures of avian tubercle bacilli. He clearly proved the existence of this immunity by comparing the results of inoculation of virulent bacilli into the anterior chamber of the eye in immunized and non-immunized animals.

This may fairly be regarded as the first clear demonstration of an appreciable degree of artificial immunity against tuberculosis.

In Dec., 1894, de Schweinitz§ published an account of the successful immunizing of guinea-pigs by inoculation with a culture of human tubercle bacilli attenuated by cultivation upon artificial media through twenty generations. In 1896 he claimed to produce a relative immunity in cattle by the same means. He also showed that some cows resisted successfully small amounts of the above culture when introduced by intravenous inoculation.

McFadyean‖ proved that cattle differ from each other in their power of resisting the tubercle bacillus, and succeeded in increasing this natural resistance by repeated inoculations of a culture of avian bacilli.

Pearson and Gilliland** demonstrated that cattle may be refractory to intravenous injections of large quantities of a culture of tubercle bacilli obtained from human sputum, and that if these injections are repeated, such a degree of immunity may be developed that *these* cattle successfully resist doses of a virulent culture of a bovine bacillus that is fatal for the control animals.

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* Bull. de l'Acad. de Med., Oct. 29, 1889.

† Annales de l'Institut Pasteur, 1890.

‡ New York Med. Jour., July 23, 1893.

§ Med. News, 1894. U. S. Dept. of Agr., Bull. 13, 1896.

‖ Jour. Comp. Pathology and Therapeutics, June, 1901; March, 1902.

** Phila. Med. Jour., Nov. 29, 1902.

In 1903 Trudeau* announced one of the most important pieces of experimental work that has yet been done on immunity in tuberculosis. He used as his immunizing agent a living culture of the tubercle bacillus that had become much attenuated by long cultivation upon artificial media. It had been obtained originally in 1891 by himself directly from a case of miliary tuberculosis in man. It was then passed through a rabbit, and from this time on grown on artificial media, chiefly glycerin-peptone-bouillon.

The culture finally came to grow more rapidly than formerly, showing no marked change, however, either microscopically or macroscopically; and it produced just as efficient tuberculin at the end as it did originally. It showed, however, a gradually diminishing virulence for guinea-pigs, and after the first six years, in ordinary doses, it did not kill rabbits, and in guinea-pigs produced only very slow lesions, or in other cases did not kill the animals at all.

He administered increasing doses of this material to healthy guinea-pigs, and subsequently, inoculating these animals with a virulent culture of tubercle bacillus, was able to demonstrate a distinct difference between the lesions produced in these animals and in control animals which had not been immunized, and to which the same doses of the virulent material were given. In general, in the immunized animals the lesions at first appeared to be more extensive than in the non-immunized, but subsequently the former showed retrograde changes, while in the latter the lesions advanced steadily in the usual way until they were fatal.

Neufeld † also reports success in obtaining a certain degree of immunity in animals, chiefly asses, goats, and cows, by successive inoculations with attenuated living tubercle bacilli. He believes that it is essential to success in these experiments that living bacilli should be used.

Behring ‡ claims to have secured the highest degree of artificial immunity in cattle yet obtained. His method is as follows: He grows upon serum a culture of the tubercle bacillus that has been cultivated in his laboratory since 1895, and which has reached a high degree of attenuation. He scrapes off this culture, dries it in a vacuum, and introduces 0.001 gm. into a young cow by intravenous inoculation. After four weeks he makes another injection of 0.025 gm. These animals resist doses of virulent bovine bacilli that kill the controls in six weeks. The material has been placed on sale in Marburg, and is being extensively employed in many veterinary institutes in Germany. These experiments have been too recently made to permit of a judgment of the permanence of the immunity thus acquired.

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* Trans. of Assoc. of Amer. Phys., 1903.

† Deut. med. Woch., Sept. 10, 1903.

‡ Beiträge zur exper. Therapie, 1902, and Berlin. klin. Woch., Mar. 16, 1903.

Behring* believes that immunity in man may ultimately be secured by two methods: (1) Isopathic immunizing by inoculation with attenuated non-pathogenic cultures of the bacilli. (2) By treatment with anti-bodies.

He regards as hopeful the possibility of immunizing man by feeding with the milk of highly immunized cows.

From the above experiments it will be seen that the fact has been established beyond question that an appreciable degree of artificial immunity can be developed in some susceptible animals by repeated inoculations with attenuated living cultures of the tubercle bacillus. But up to the present, none of the many attempts made to produce a toxin immunity have been successful.

The field, then, is promising enough to justify the extensive experiments that are being carried out in it, and there is some hope that results favorable to the control of the disease in man may ultimately be achieved.—Ed.]

The **inhalation of compressed air** in pneumatic cabinets or by Waldenburg's apparatus has been often recommended. An experience of many years with the cabinets in Reichenhall does not lead me to indorse this opinion. There is no evidence of any effect upon the course of the tuberculous process. It can only be of use in absolutely stationary forms, if there is at the same time marked swelling of the bronchial mucosa and severe bronchial asthma. In such cases I have at times seen fairly favorable symptomatic results. A. Schmid, who also had a wide experience with this method, came to the same conclusion.

Expiration into **rarefied air** is generally regarded as useless. It is perhaps not entirely without danger, inasmuch as it works to a certain extent like a leech, and may induce a rupture of a vessel.

The inhalation of **hot dry air** (Halter, Weigert), also of moist warm air, was soon abandoned.

The **electrical treatment** of consumption was recommended by de Renzi, but does not seem to have come into general use. A large zinc anode with a cushion soaked in 10 per cent. bicarbonate solution, and a negative pole dipped in a 5 per cent. solution of potassium tartrate, are used; strength of the current, up to 120 m.a.

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* Berlin. klin. Woch., Sept. 24, 1903.

Röntgen Rays.—Lortet and Genoud inoculated guinea-pigs and submitted the site of inoculation to the action of the rays for at least one hour during two months. These animals developed no abscesses, the inguinal glands were hard and of normal size, and the animals were in good condition, whereas the controls developed purulent ulcers and soft cheesy inguinal glands, and were considerably emaciated. Fiorentino and Linaschi also believe that the development is greatly delayed in animals. Rieder exposed cultures of tubercle bacilli to the rays, and came to the conclusion that they were probably affected.

A certain reinforcement of the natural tendency of tuberculous foci to heal up might conceivably be effected by mechanical means—far more easily of foci in the extremities, indeed, than in the inaccessible lung.

We have previously indicated that the natural process of cure depends upon the fact that the poisons, instead of being absorbed, become aggregated in the periphery of the tuberculous focus (poison zone), where they stimulate the tissues to indurative changes, and thus isolate the focus and prevent the dissemination of the bacilli by the lymph-channels.

If it were feasible, by obstruction of the efferent lymphatics, to induce just the proper degree of concentration of the poisons, the process of cure would be very materially advanced. This would represent a form of the tuberculin treatment, with the double advantage that the tuberculin manufactured in the body itself is applied directly at the site of its origin, and that the healthy tissues of the body are not also implicated, as with the injection treatment, but are actually relieved of the poison which they would otherwise absorb.

Mention may be here made of **Bier's method** of curing tuberculous foci, especially those situated on the extremities, by means of congestive hyperemia, which has a certain analogy with the preceding idea, although based upon different premises.

Bier went on the assertion of Rokitansky that cardiac lesions causing congestion of the lungs and likewise spinal curvatures conferred a certain degree of immunity against tuberculosis, inasmuch as the autopsy of such persons disclosed either no tuberculous lesions or only healed foci. Although this theory was not confirmed by the autopsy records of Frommolt and Schultze, it yet found many adherents among clinicians (Bamberger, Traube, von Dusch, Rühle, Quincke). As a partial complement to this theory, the cases of pulmonary stenosis, which condition a lowered vascular supply to the lungs and undernutrition, are credited with a predisposition to tuberculosis (Farre and Travers, Louis, Lebert, Eymann, Heller).

The conditions of this supposed immunity were imitated by Bier, first by improving the arterial flow to tuberculous limbs and also by inducing an active hyperemia by sweat baths. The results in the way of improvement or cure were, however, entirely negative. He then tried passive venous hyperemia, which he induced, following Helferich's suggestion, by a sort of incomplete Esmarch ischemia; the bandage is put on too loosely to arrest the arterial flow, but tight enough to impede the venous return.

The diseased extremity is carefully bandaged to just below the lesion, and immediately above it is applied a rubber bandage so firmly that there is marked peripheral stasis. To avoid pressure, the position of the bandage is changed twice daily. The constrictor should never cause pain, vesiculation, atrophy, or decubitus; under these circumstances it may be continued for days and weeks, and is not contraindicated even by peripheral edema. If circumstances permit, the patient should be out of bed.

Bier believes that the curative effects are due less to an increase of nutrition in the part than to the actual venous stasis, which induces connective-tissue proliferation and cicatrization with inflammatory reaction—just as Landerer explains his cinnamic acid, and Liebreich his potassium cantharidate.

This explanation of Bier's does not seem to me plausible. Heller regards the retention of the metabolic products of the bacteria as the essential factor, which I believe to be nearer the truth. Only, I do not consider the toxic effects of these upon the bacteria as the *modus agendi*, but rather their irritation of the tissues and the consequent peripheral cicatrization.

Inasmuch as the Bier method, even though unintentionally, induces a marked obstruction of the outgoing lymph and proteins, it is easy to understand that Bier and a host of imitators (Zeller, Mikulicz–Henle, etc.) obtained very good results, sometimes after preliminary exacerbations, especially in tuberculosis of the joints, the epididymis, and the testicle.

That the method is not successful in every case is due chiefly to the fact that compression is directed against the veins instead of the lymphatics, and that just a certain degree of concentration is necessary to obtain the desired effect. If this is too weak, the tissues are not sufficiently irritated to prevent the dissemination of the bacteria.

If it is too great, suppuration occurs, just as in the injection of dead bacilli in concentration into the tissues. As a fact, Bier has observed cold abscesses in a number of cases,* which I consider attributable to too strong a concentration; Bier, also, in the further elaboration of his method, has abandoned continuous compression; Mikulicz requires only fourteen to eighteen hours in the day.

A further source of failures might be that the bandage, owing to an imperfect demarcation of the focus, did not stop above it, but compressed it and so drove a quantity of protein into the general circulation. I believe, therefore, that the extent of the focus should previously be determined by the *x*-rays.

A method which produces lymphatic stasis proximal to the tuberculous focus, without injury to the rest of the organism, is undoubtedly rational, but is applicable only in case of involvement of the extremities or the testicle.

SURGICAL TREATMENT.

The attempt has also been made to apply surgical methods to the treatment of tuberculosis.

Mosler (1873) first tried the injection of carbolic acid and salicylic acid into the lung; also, in one case, the operative opening of a bronchiectatic cavity.

In 1881, Gluck, H. Schmid, Block, and later Biondi, showed that the resection of portions of the lung and even the extirpation of one lung was survived by animals. Further experiments were made by W. Koch, Rochelt, C. Spengler, Kurz, and Reclus.

Sonnenburg tried the surgical treatment of tuberculous cavities in conjunction with the injection of tuberculin, but had just as little success as other authors. Recently Terrier, Franke, Tuffier and Quincke have given their attention to pulmonary surgery, not, however, with reference to tuberculosis alone.

Surgical interference cannot be credited with any influence upon the therapy of tuberculosis. The failure of the operation is not due to technical difficulties; these could easily be overcome. Lung tissue, formerly regarded as a *noli me tangere,* has not proved so, aside from the danger of entrance of air into the veins. The real danger of a pleurisy or a pneumothorax may be obviated by the artificial induction of adhesions between the leaves of the pleura by means of suture, the Paquelin cautery, or zinc paste, unless, indeed, these are already present. The chief difficulty is the accurate localization and demarcation of the focus, which the most careful physical examination and even radiography do not suffice to accomplish. Even restricting the operation to apparently primary and isolated foci, it is impossible to surmise whether and to what extent dissemination of the bacilli has occurred. In view, therefore, of the possibility of recovery through hygienic and dietetic measures, one should always hestitate to invoke surgical intervention with its difficulties and doubtful outcome, the more so that one cannot be sure of operating in healthy tissue, which is a preliminary requisite, and so runs the danger of disseminating the tuberculosis.

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* These were treated with 10 per cent. iodoform glycerin.

The operative treatment of cavities, with the intention of giving vent to the detritus and the products of mixed infection, has also had little success. Aside from the possibility of a complicating gangrene, the chief danger, namely, the infiltrated wall with its living bacteria, still remains behind; lastly, there is the possibility of a permanent pulmonary fistula.

Simple puncture and irrigation of the cavities would be a small operation, assuming the presence of adhesions. But the method seems to me to forfeit an advantage which nature has provided, namely, the thickness and viscosity of the cavity contents; the thin disinfecting media mingled with the bacilli, are easily carried to other parts of the lung, the fluid portion is absorbed, and the bacillus, not so rapidly influenced by the disinfectant, remains and proliferates. Even the intraparenchymatous injections, which at times offer the same advantages as the irrigations, seem to us of no theoretical value, nor are they justified by practice.

In uncontrollable hemorrhages little help can come from the surgeons, since the bleeding point is not to be determined with accuracy. At most, we might consider the artificial induction of pneumothorax, either complete or incomplete, by forcing air into the pleura; or, with better prospect of success, Tuffier's suggestion of resecting an upper rib, with the intention of causing the collapse of a definite area of lung over the site of hemorrhage. The latter procedure has also been suggested for cavities, with the idea of causing contraction by approximation of the walls, and is rational in so far that a large cavity, held in distention by negative pressure, not only tends to aspirate bacteria, but constantly menaces hemorrhage from the stumps of vessels in its walls.

[It cannot be said that the surgery of pulmonary tuberculosis has established its claims to recognition during the past three years.

While a few surgeons (Wills,* Sarfert,† Landerer,‡ and others) advise operations in certain cases, others (Verneuil,§ Whitacre||) regard them as hardly justifiable. The procedure is not one that will commend itself to physicians of extensive post-mortem experience, for at the autopsy table it is extremely uncommon to find a solitary focus of tuberculosis in the lung, except in the early stage, when operation is not practicable, and when climatic and out-of-door treatment offer the best hope of recovery.

In advanced cases, with breaking-down of a tuberculous area, there are almost invariably secondary foci scattered through the lungs, and often undiscoverable by physical examination.

Moreover, the improving results of medical treatment, even in these advanced cases, render surgical procedures less and less desirable.

A method of producing collapse of the lung was proposed and tried by Murphy.** He points out that tuberculous lungs that have collapsed by reason of pleurisy with effusion, pneumothorax, or operations on the chest wall, exhibit a tendency to heal.

Reasoning from this, he concludes that many cases of phthisis would be benefited or healed if such a collapse could be brought about safely. Murphy's method is used as follows: An ordinary aspirating needle is sterilized and attached by a sterile rubber tube to a glass vessel containing sterile absorbent cotton, through which the gas is to be filtered. This, in turn, is attached to a small gasometer, by means of which the amount of gas injected can be measured and the pressure regulated. The chest-wall having been prepared, the needle is forced just through the parietal pleura, and the patient directed to take a long breath, which generally starts the flow. From 50 to 200 cubic inches of gas is introduced, or until the lung has collapsed and no breathing sounds can be heard over it.

The needle is now withdrawn, and a firm pad placed over the puncture to prevent subcutaneous emphysema, an accident which fairly often happens.

The patients complain of some pain and dyspnea, but generally soon become used to the changed condition. The gas is not absorbed, but is withdrawn by an aspirating needle after several months. *X*-ray examination shows the lung to be collapsed.

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* Jour. Am. Med. Assoc., Jan. 5, 1901.

† La Semaine Med., 1900, No. 50.

‡ Münch. med. Woch., 1902, No. 47.

§ Annales de la Soc. Belge de Chirurg., 1900

|| Jour. Am. Med. Assoc., 1902, xxxix, 748.

** Jour. Am. Med. Assoc., July 23, 1898.

The most favorable cases are those with lesions of moderate extent and not of long standing, limited to the apex and without adhesions. Chronic cases of long standing or far-advanced cases are not suited to it.

Although some successes have been reported, there have been many failures, and the procedure has proved to be by no means free from serious risk. On the whole, cases that would be suitable for this plan of treatment would have a better chance of recovery under climatic and fresh air management, and consequently the method has failed to gain the confidence of the medical profession.—Ed.]

SYMPTOMATIC TREATMENT.

FEVER.

Of all the symptoms, fever gives us most trouble. It is not only a valuable diagnostic sign, but furnishes a criterion of the progress of the disease throughout. We know that a rise of temperature denotes an advancement of the process, and that only normal temperature offers hope of recovery.

To avoid repetition, I refer to the foregoing chapter. We there argued that the cause of fever was the absorption of the proteins of the tubercle bacilli and of the secondary bacteria, and indicated the necessity of two-hourly measurements (see pages 384 and 460).

For the febrile cases, in addition to change of climate and fresh air, absolute **rest in bed** is necessary; for those with severe fever, actual "cadaveric rest" is indicated, and is an extremely important element of the entire therapy. The fever in itself denotes loss of body-substance; if to this is added still further loss through movement, every particle of which costs albumin and fat, the loss is, as a rule, too great to be covered by the nutritive processes, which are depressed by the fever. The inevitable consequence is a dissolution of the body-substance, and an increased absorption not only of fat and albumin, but also of the proteins, which set up more fever. It is, above all, important to break this *circulus vitiosus.*

The damaging effects of activity can easily be discerned in the temperature curves of patients with fever or with labile temperatures, often, however, not unless the temperatures are taken every two instead of every four hours. Every increase of exertion, every premature attempt to get up is manifested by an evident rise of temperature, generally at once, sometimes only after one or two days. I have already stated that birthdays, joyful or sad letters, visits, and manual occupation may be recognized as a cause of irregularities in the temperature curve.

Brehmer's rich experience—and his two-hourly measurements—taught him the great value of rest in bed in case of fever. Volland and others have urged it at intervals. To the detriment of the patient, however, it is far too rarely carried out. Many obstacles stand in the way of it. The patient himself, especially if the fever is moderate, objects to going to bed; either he does not feel sick enough or because he wishes to avoid the appearance of sickness, because he dreads the tedium of it, because he is impatient of the restraint. A still greater obstacle at times is the resistance offered by the relatives and companions, on whom there would be an increased demand, which they could not decently refuse and which would seriously interfere with their habits and pleasures. All sorts of devices are resorted to; the physician is asked whether the patient "can not get up yet," or the latter is actually allowed to get up on the sly. Yet the physician must enforce his demands by various devices—by instructing the patient, by persisting, by an occasional sharp reproof.

The objection that rest in bed weakens the patient is only apparently justifiable. An invalid, like a healthy man, shows a certain weakness of inaction upon first getting up after a few days of confinement in bed, but this rapidly disappears.

A real disadvantage, however, is the room-confinement and the loss of fresh air, which is really most important to a febrile case. This is the chief cause of the bad results (*e. g.*, loss of appetite), which come from confinement to the bed, especially in the older hospitals. The vitiation of the air and the circulation of dust may in part be remedied by better ventilation and moist cleaning; the radical cure, however, is to carry the patient in his bed, properly covered, into the open air. A balcony, well protected from wind and rain, lends itself excellently to this purpose. Unfortunately, this essential is generally lacking in the health resorts and even in the sanatoria. Only in case the conditions of the dwelling are absolutely unfavorable, in case the window opens on a narrow alley or a court, and when, at the same time, the fever is only moderate, can one weigh the question whether the invalid suffers greater harm from the loss of air or from the exertion of being up.

In all cases with a tendency to hypostatic congestion, or in very debilitated invalids, bed-rest is to be advised with a certain amount of reserve; in hopeless cases, if they object, it may be excluded. In general, even slight degrees of fever, a rise beyond 37.5° C. (99.5° F.)

in the axilla, indicate confinement to the bed. If the temperature again becomes normal, one ordinarily waits three days, and then allows the patient to get up, at first only for one hour during the day, at a time when the temperature is normal. He must avoid unnecessary exertion. The time out of bed is then extended by one-half to one hour every day "*in refrecta dosi*"; the least rise indicates bed-rest again for one or two days. Compromises, *e. g.*, allowing the patient to lie on the sofa with his clothes on, are not permissible. The invalid never rests as well in clothes as without, he is less comfortable on the usual poorly constructed sofa than on a bed, and, finally, he is much more apt to undergo little exertions—*e. g.*, to fetch this or that.

If the fever lasts only one or two hours in the afternoon and is not high, say up to 37.7° C. (99.8° F.), the patient is often allowed to get about in the morning, when he is afebrile. The rationale of this has never been clear to me. The tuberculin injections, which in many respects mimic the absorption of proteins, cause a rise of temperature in six to sixteen hours, varying with the case, and on their analogy we are entitled to assume that the conditions responsible for the afternoon temperature fall within the morning and forenoon hours. The exceptional cases in which consumptives go about for a long time in spite of considerable fever cannot justify us in advising a measure which raises fever by furthering the absorption of the proteins.

There are occasional exceptions to this rule. Sometimes, as in the chronic fever of cavities, the temperature is obstinate; here, one may cautiously try getting up.

It may take months and years before the temperature becomes normal again. Such cases demand great circumspection and care on the part of the physician, and much patience, insight, and forbearance from the patient. Many years of experience have taught me that timely use of the rest cure gives astounding results even in old cases.

In addition to rest in bed, the fever is to be combated, according to Brehmer's suggestion, by the use of **alcohol.** It is best to give a wineglassful (150 cc.) of strong wine (about 8 to 12 per cent. of alcohol) at the onset of the more rapid rise, and a second similar dose upon a second rise. One should avoid too large doses.

Alcohol is also the best treatment for the occasional initial chill; in order to anticipate the first feeling of chilliness, one administers a glass of hot toddy or of mulled wine one hour before the time of the expected chill, reckoning by the previous day, and then keeps the patient thoroughly covered up. I hold it important to keep the head especially covered, so that only the eyes, nose, and mouth are free. In this wise one may often not only prevent the chill, but also lower the subsequent fever.

If the fever is high, the patient often experiences relief from the application of a **cold compress** or an **ice-bag** to his head, or from sponging with a cloth or sponge dipped in cold water or dilute vinegar. For this, however, one should wait at least an hour after the last feeling of chilliness has passed off. If the chill comes in the morning, the patient is provided with warm water for washing, all his needs are attended to in bed, and cold drinks are forbidden him, in order to avoid every possible variation in temperature, which might act as an exciting cause.

Arsenic has been recommended for the chill (Powell, Pollack).

The use of alcohol is reinforced, according to Brehmer's example, by laying an ice-bag upon the heart, which in many febrile cases tends to induce sleep. In cases of chill the ice-bag must be discontinued one hour previously and at least one or two hours afterward.

The **fever diet** depends chiefly upon the condition of the digestive organs. If these are normal, the ordinary diet may be given even with high fever. If there is anorexia or the gastro-intestinal functions are impaired, as is frequently the case, especially in the first days of an acute febrile attack, one employs the diet previously described under the treatment of anorexia: porridges, milk, Gärtner's fat-milk, barley soups, gelatinous foods, jellies, later finely chopped meats, hash with vegetables, ragouts, with the addition of the various nutritive preparations, possibly supported by the different stomachics. In the first days of the fever one gets along with 20 to 25 calories per kilo (von Noorden), but this must be increased to 30 to 35 in chronic fever, or even higher. Cooling of the food and drinks tends to lessen the feeling of heat. The wet full rubs are omitted in febrile cases. Pharmaceutical preparations had best not be used, unless one is compelled by the impatience of friends and relatives to invoke their moral effect. Very high fever, also, according to modern views, justifies their use. I have only rarely seen any actual benefit to the patient. The temperature is, indeed, brought down by sufficiently large doses, but other phenomena—*e. g.*, sweats, often more weakening and depressing than the fever itself—take its place, so that the patient no longer asks for them. In small doses they often have a favorable effect upon appetite and sleep, but prolonged use has compensating disadvantages. The choice of drugs is not important; if one fails, another may be selected.

Antipyrin (1 gm. repeatedly) often deranges the heart, occasionally induces collapse and severe sweats, which may be averted by a little atropin or agaracin one-half hour before the first dose. In Görbersdorf in 1885–86 antipyrin was freely prescribed, but the actual benefit was slight. Eichhorst gives antipyrin 2.0 to 4.0 in water 50.0, as an enema.

Others recommend **phenacetin** in doses of 1 gm.; others, especially when there is cardiac weakness, use **quinin.** Jaccoud gives it as the hydrobromate, on the theory that it is less irritating to the stomach; since quinin exerts its full action six to eight hours after being taken, he gives it seven hours before the rise; he gives 1.5 to 2 gm. on the first day, 1.5 on the second, and 1 on the third, to be taken within fifteen to twenty minutes; after two or three days' intermission the course is repeated, if necessary. Niemeyer gave quin. sulph. 2.0, pulv. dig. 0.5, extr. gent. 9.0, fiant pil. no. 40; six to ten pills daily. To disguise the taste, it is given in England dissolved in milk (5 dcg. quin. hydrochlor. in 300 of milk is almost tasteless). Or, one may give an enema of—

℞.	Quin. hydrochlor.	1.0
	Aq. dest.	100.0
	Tinct. Opii Simp.	x
M.	Sig.—For two enemas (v. Szekely).	

In diarrheal tendencies quinin is to be avoided.

Sodium salicylate is recommended, 3 to 6 gm. a day. Also lactophenin (0.5 to 1.0), which is also a sedative and hypnotic.

I still prefer antipyrin (0.2 to 0.3) three or four times a day, at a time determined by the onset of the fever. Von Jacksch gave as much as 6 gm. a day, but smaller doses have frequently been known to produce icterus (Witthauer) and vertigo (Wefers).

The chief thing is always to give the antipyretic at the proper time, *i. e.*, before the fever has begun to rise. It is therefore ill advised to give the drug every two to four hours or two to four times a day. One must actually lie in wait for the first indication of the rise, and then drive home with the medicine. The irregularity of the fever makes it difficult to hit the time exactly, since the doctor cannot always be present in person and rarely can trust his nurse sufficiently. Moreover, our instruments are not perfect enough for the purpose; if we had permanent thermometers, which registered the temperature automatically, we should be better able to manage it. In a few cases, which were cared for by very intelligent and obedient mothers, I found it possible to hold the temperature in check by well-timed doses of 0.05 to 0.1 of antipyrin a day, *i. e.*, minimal doses. All in all, I consider it wiser to proceed cautiously, lowering the temperature a fraction of a degree by small doses, rather than to dose heroically.

NIGHT-SWEATS.

These are not an inevitable accompaniment of fever, although in hectic they often coincide with the subnormal phase.

The treatment demands that the sleeping-room should be cool and that the window should be about half, or, if possible, wide open; drugs are then often superfluous. The patient should not be too well covered, for if the limbs lie close to each other they are kept warmer and tend to perspire more easily. The arms are to be kept outside of the coverlets, and if the patient feels cold, they may be separately covered. The lower limbs, too, up to the perineum, are to be separated by a light cloth or by wide pantaloons. The patients often help themselves by frequently airing the bed-clothes, but this should be done cautiously.

If this does not suffice, a glass of cold milk with two (at most three) teaspoonfuls of cognac may be taken at night. Now and then, eating a piece of buttered bread upon awaking at night serves the purpose (see page 398). During the sweat the patient is benefited by being rubbed with a coarse, dry towel, followed by sponging with cold water or with vinegar (in which one may dissolve a teaspoonful of red pepper to the cup), or with French brandy; change of linen and bed-clothes is also very grateful. Likewise powdering with salicylic acid, which may, however, cause severe cough.

℞.	Acid. salicyl.	3.0
	Amyl.	10.0
	Talci	87.0

M. Sig.—Powder, after oiling the skin.

Persistent fresh-air treatment generally cures the sweats with the improvement in the general condition. Among drugs, atropin, further agaricin, cotoin, extr. hydrast., etc., are most used.

℞.	Atropini sulph.	0.01
	Boli albi	q. s.
	Aq. dest.	q. s.

Ut f. pil. No. 40.
Sig.—Two to four pills at night.

Or—

℞.	Atropini sulph.	0.01
	Aq. laurocer.	10.0

Sig.—Ten drops at 6.00 P. M.; if necessary, also at night.

Or, in case of digestive disturbances, subcutaneously:

℞.	Atropini sulph.	0.1
	Aq. dest.	10.0

M. Sig.—One hypodermic injection at 6.00 P. M.; at night also, if necessary.

Or—

℞.	Agaricini	0.1
	Pulv. Doveri	2.0
	Rad. Alth.	
	Mucil.	āā 1.0

F. pil. No. 20.
Sig.—One pill in the afternoon and one in the evening.

(Often works only six hours—Seifert; therefore in morning sweats best given after midnight; often causes indigestion.)

℞.	Cotoini	0.5
	Sacch. pulv.	5.0

Div. in dos. No. 12.
Sig.—A powder at 8.00 and one at 10.00 P. M.

(Especially in cases with diarrhea.)

℞.	Extr. hydrast. (or Hyoscyami)	0.01
	Aq. dest.	10.0

M. Sig.—Half of above hypodermically.

℞.	Cotoini	0.5
	Aq. dest.	150.0
	Syrupi	20.0
	Spir. dil.	10.0

M. Sig.—At 8.00 and at 10.00 P. M. one teaspoonful.

℞.	Sol. arsen. Fowleri	
	Tinct. bellad.	āā 3.0
	Aq. laurocer.	20.0

Sig.—Fifteen to twenty drops at 6.00 P. M.; if necessary, also at night (v. Szekely).

Further, camphoric acid (fairly reliable) 1 or 2 gm. in powder (Fürbringer); picrotoxin 0.015 (Cauldwell); potassium tellurate 0.02 to 0.04 (Neusser); sulfonal 1 to 2 gm. at night; lead acetate 0.02 in powder. Formerly salvia tea and Boletus laricis were in high repute.

COUGH, EXPECTORATION.

Cough, in so far as it serves to remove the secretions, is, within certain limits, a beneficial reflex, with which it would be irrational to interfere. Frequently, however, it is unnecessarily severe, and ought to be lessened or assuaged. Severe cough irritates the respiratory mucosa, disturbs sleep, and depresses the mind; it leads to vomiting, weakens the body, and may induce emphysema, rupture of the blood-vessels, and hemorrhage or pneumothorax. The forced inspirations which follow excessive coughing may easily occasion the aspiration of sputum with a consequent aspiration pneumonia and tuberculosis —sufficient grounds for combating the symptom.

Fortunately, the reflex is to a great extent under the control of the will. The consumptive must learn that he can control excessive cough, especially that he need not yield to empty cough, which does not serve to eliminate the secretions, for every act of coughing is a fresh source of irritation. If he withstands the first impulse to cough, this generally disappears of itself, and the sputum, or whatever caused it, is eliminated without effort. The first measure against cough, therefore, is this mode of training, introduced by Brehmer, and its efficacy is demonstrated in the sanatoria, where, in spite of the many patients, there is remarkably little cough, and at table scarcely any. It often does well to advise the patient to smother the impulse to cough by making about ten very slow inspirations and somewhat more forcible expirations. If this is too much for the strength of will of the patient, we are forced to resort to other measures, which depend largely upon the cause and the site of the irritation.

The patient must seek pure air and avoid dust and smoke (including cigar smoke). He protects himself against dusty or cold irritating air by holding up a cloth before his mouth. Moist warm air is most beneficial. The air of the room may be sufficiently saturated with moisture by placing a bowl of water on the stove, or by strewing about solutions (1 to 2 per cent.) of common salt or sodium bicarbonate. If the patient has difficulty in getting rid of his sputum in the morning upon awakening, a glass of very warm water ordinarily helps him. Solution of the secretions is best assisted by the lukewarm alkaline waters, *e. g.*, Selter or Neuenahr, each, with whey or milk, or alone, one or two glasses in the morning, if necessary also in the evening; or a course in some suitable place (Reichenhall, Ems, Gleichenberg, Lippspringe, Soden).

A swallow of hot or cold water (*les extremes se touchent*) is particularly good for irritation in the throat, or a piece of sugar with a few drops of cognac or arrac (moderation!), or slowly sucking a half or a quarter pastille (Soden, Ems), Iceland moss, licorice, salmiac, or Löfflund's or Stollwerk's malt-bonbons; only, the patient must be warned not to chew pastilles all day long, and so destroy appetite and digestion.

Cough dependent upon catarrh of the respiratory mucosa is often relieved by the **inhalation of salt water** or of the natural alkaline waters.

The prejudice against inhalations is unjust. J. Schreiber has indeed shown that medicaments in pulverized form do not penetrate to the diseased areas of lung—to the tuberculous focus—since this does not breathe, but they do reach the mucous membrane of the finer bronchi in the same way as dust. This is also proved by the experiments done under my direction by Dr. Fränkel (Badenweiler). Inhalations of tuberculin by means of Jahr's apparatus produced the same reaction as did the same dose when given by injection, ample evidence of the absorptive capacity of the respiratory mucosa. It is impossible to ascribe the reaction to the swallowing of the tuberculin, since the administration of such doses per os is well known to be without effect.

The sanatoria usually have large rooms for inhalation; the danger of infection, according to my investigations, is nullified by the pronounced humidity of the air. Penzoldt thought highly of the drying-houses in which the moist salt air could be taken in the open (*e. g.*, Reichenhall, Salzungen); my own experience does not confirm this.

Inhalations of lignosulphite were credited with a specific action upon tuberculosis by their discoverer, Hartmann. This has not been confirmed by the subsequent investigations of Heindl and others; isolated cases showed, in addition to an increase in appetite, an improvement in breathing, attributable to the action of the sulphur acids upon the swelling of the mucous membrane. Lignosulphite is contraindicated by a tendency to hemorrhage, as it frequently causes bleeding.

One cannot entirely avoid the use of drugs for the cough, but should be sparing with them, in order that they may not prove worthless in time of need, *sub finem;* it is well, therefore, to use the weaker drugs first. Von Szekely prescribes, in order of strength: cannabis indica, gelsemium sempervirens, hyoscyamus, paraldehyd, codein, morphin, and opium.

℞.	Extr. Cann. indicæ	0.5
	Sacch. alb.	5.0

M. F. p. Div. in dos. x.
One powder three times daily.

℞.	Extr. Cann. indicæ	0.5
	Emuls. oleos.	200.0

One dessertspoonful every two hours, after shaking.

℞	Tinct. gelsem.	10 0

Sig.—Five to ten drops, three times a day.

℞.	Extr. hyoscyami	0.5
	Aq. lauroc.	10.0

Sig.—Ten drops every three hours.

℞.	Extr. hyoscyami	0.5–1.0
	Sacch. alb.	5.0

M. F. p. Div. in dos. x.
One powder three times a day.

℞.	Paraldehyd	5.0
	Decoct. Alth. (e 15)	150.0
	Succ. liquir. dep.	20 0

M Sig.—One teaspoonful every two hours.

℞.	Codein phosph.	0.3
	Cognac	10.0
	Syrup. simpl.	90.0

M. Sig.—One teaspoonful three to six times a day.

℞.	Codein phosph.	0.3
	Aq. lauroc.	10.0

M. Sig.—Ten to twenty drops three times a day.

℞.	Codein phosph.	1.0
	Extr. gent.	
	Pulv. rad. liquir	āā q. s.

F. pil. Nr. 30.
Sig.—One pill two to three times a day.

℞	Extr. opii	0.1
	Elæosacch. menthæ	5.0

Div. in dos. 12.
Sig.—One powder three times a day.

℞.	Morph. muriat.	0.05.0.1
	Aq. lauroc.	10.0

Sig.—Five to twenty drops three times a day.

℞.	Morph. muriat.	0.05
	Sacch. alb.	5.0

Div. in dos. 10.
Sig.—One powder every three hours

Codein is especially well liked, not only because it lacks the constipating tendency of opium and morphin, but also because it does not so easily induce the opium habit. Prolonged treatment demands constant change. It is best not to give the patient definite orders as to the time of taking, *e. g.*, every two hours, etc., but to determine the maximum of the daily dose, and to adjust its distribution according to the severity of the attack.

Moist warm applications (Priessnitz) to the neck and chest are of value. Gross changes in the neck and throat are treated locally. Catarrh of the nasopharynx particularly often gives rise to unbearable hawking, coughing, and vomiting, especially in the morning. A good method is to paint locally with iodin and potassium iodid in glycerin—iod. pur. 0.1 to 0.3, potass. iodid. 1 to 3, glycerin 10.0—every one or two days; the nasopharynx must be included, and the treatment should, therefore, never be left to the patient.

Insensitiveness of the epiglottis, which permits the aspiration and invasion of saliva during the night, demands *electrical treatment* and cautious stimulant applications. For the cough of laryngeal catarrhs, in addition to the internal use and the inhalation of the alkaline waters, dusting or painting with narcotics (5 per cent. cocain locally) are in order, unless the presence of tuberculous processes indicates other measures. For croupy cough, which is produced, especially in children, by swollen bronchial glands, we may rub in soft soap locally and give potassium iodid internally.

The secretions are loosened by exercise in the open air and easy climbing, by the internal use of warm water and salt springs, especially the Lippspringe Arminius water, by inhalations and moist warm applications to the chest (the "cross bandage"). The so-called expectorants are rightly regarded with suspicion; their prolonged use is excluded, under any circumstances, by their disagreeable effect upon the appetite and digestion. Ipecac, apomorphin, antimony preparations, and, in case of profuse secretions, senega and ammonium carbonate are the drugs to be considered.

℞.	Inf. rad. ipecac.	0.3–0.5 : 150.0
	Syr. cort. aur.	15.0

M. Sig.—Four to five dessertspoonfuls a day.

℞.	Apomorph. muriat.	0.03–0.06
	Morph. mur.	0.01–0.03
	Acid. mur. dil.	0.5
	Aq. dest.	150.0
	Syrup. cort. aur.	20.0

M. Sig.—One dessertspoonful every two to four hours.

℞.	Sulf. aurant. antim.	0.3
	Sacch. alb.	3.0

M. F. p. Div. in dos. 10.
Sig.—One powder every three hours.

℞.	Decoct. rad. althææ	200.0
	Syrup. ipecac.	20.0

Sig.—One dessertspoonful every one or two hours.

℞.	Inf. rad. seneg.	10 : 200.0
	Oxymell. scillæ	5.0
	Syrup. cap. ven.	20.0

Sig.—One dessertspoonful hourly.
(Or senega with potass. iodid. 5.0.)

℞. Succ. liquir. depur.
Liquir ammon. anisat. .... aa 15.0
Aq. fœnic. 50.0
Sig.—One teaspoonful three or four times a day.
Mistura solvens stibiata:

℞. Ammon. muriat. 5.0
Tart. stibiat. 0.05
Aq. fœnic. 180.0
Succ. liquir. 10.0
M. Sig.—One dessertspoonful every two or three hours.

Narcotics may be added to the above if necessary.

In order to diminish the secretions, which are often so profuse as seriously to incommode the patient, we may employ inhalations with oleum pini pumilionis, Mack, with oil of turpentine, particularly if the sputum is fetid, with oil of eucalyptus and the other ethereal oils (10 to 20 gtt. in a glass of hot water, inhaled), also balsam of Peru, oleum salvæ, tinctura benzoini, or tinctura myrrhæ 2 per cent.; solution of tannin three or four times a day is also recommended (Penzoldt). Internally, the favorite drugs for the purpose are creosote carbonate (creosotal) and guaiacol carbonate (0.5, one powder t. i. d.), creosote (vid. sup.), also oil of turpentine (10 to 30 drops in gelatin capsules). Likewise, balsam of Peru 10 to 30 gtt. daily in gelatin capsules (and balsam of copaiba, 30 to 60 gtt.).

℞. Terpin hydrat. 3.0
Sacch. alb.
Gummi arabic. .... āā 1.0
F. c. aq. pil. 30.
Sig.—One to four pills three times a day.

℞. Myrtol. 1.50
Exhib. in caps. gelat.
No. 10.
Sig.—One capsule night and morning.

℞. Benzolol 0.5
Elæosacch. menth. pip. 0.3
M F. p. Dentur tal. dos. No. 10.
Sig.—One powder three times a day (Eichhorst).

HEMOPTYSIS.

In connection with hemoptysis the patient must be warned to avoid everything which may occasion it, namely, every form of severe physical and also mental exertion, namely, shouting, singing, excesses in *Baccho et Venere*, the immoderate use of coffee, tea, and hot drinks, the inhalation of irritant fumes, and prolonged exposure to the sun in summer. In cases of hemoptysis, pleuritic exudates should be attacked only with great caution, since their evacuation is often attended with hemorrhage, Fränkel having had one case which resulted fatally.

Certain cases, especially those with a very acute course and rapid disorganization, exhibit an increased friability of the vessels and a sort of hemophilia. This may be due to the action of certain secondary bacteria. Inasmuch as hemorrhages often occur suddenly and we can never estimate the immediate danger of rupture, it seems to me that von Ziemssen's recommendation of gymnastic exercises even in the early stages upon the bars, etc., is extremely questionable. It is based upon the unfounded theory of the favorable influence of deep respirations. Objections to this theory are set forth on page 548. We are equally justified in assuming that the well-known demand of the tubercle bacillus for oxygen is satisfied by means of these deep respirations, and its growth correspondingly furthered.

The differentiation between pulmonary and other forms of hemorrhage has already been given (pages 370, 453). It is impracticable to vary the treatment according as the hemorrhage is due to stasis, necrosis, or other causes, as Dettweiler suggests, since the differentiation of these conditions, as he himself admits, is difficult and frequently impossible.

Considerable hemorrhages often announce themselves days in advance by the presence of traces of blood in the sputum, sharp pains in the chest, and tickling in the throat. The impending hemorrhage may then often be averted by absolute rest, by discontinuing the rubbings, by avoiding all spicy food and drink, and by depletion through the intestines.

Any especial therapy for very small hemorrhages is unnecessary. The physician should not, however, make light of them, since a greater hemorrhage a few hours or days later might place him in an unenviable light.

With severe bleedings our first care should be to calm the patient. For although some few remain entirely indifferent,—I recall the case of a young girl who, in spite of a hemorrhage of about one-fourth of a liter, continued to dance the rest of the evening,—nevertheless the majority suffer a profound depression of spirits, which, however, they often attempt to conceal in order not to discourage their friends. The physician can best accomplish this purpose by casually but firmly stating that a few days of rest and hearty feeding will easily make good the loss of blood, or, in case of women, by reminding them that they lose far more blood at the menses without suffering any especial harm.

Absolute rest, physical and mental, in bed is necessary for the arrest of the hemorrhage; the position of the patient must be such that he can easily expectorate. All talking is forbidden, and this must be impressed on those around. Prolonged physical examination, especially percussion, is useless, and actually harmful, for it is a matter of indifference for the treatment whether the bleeding comes from the right or the left lung, from above or below. But in order that its omission may not appear a matter of negligence, the physician should explain that it might at the moment be dangerous and must therefore be temporarily deferred.

Thus, I was once called for a hemoptysis by the relatives, because "the physician had not even taken the trouble to examine the case"; when I also declined to examine him, explaining the reason, they repentantly returned to their own doctor.

To arrest the bleeding and calm the excited heart, it is well to place an ice-bag over the precordium; in case the site of hemorrhage is revealed by large râles, another ice-bag may be placed here, unless, of course, the cold sets up coughing. It is usual also to let the patient dissolve small pieces of ice in his mouth. For this purpose, the ice should be artificial, since the natural ice is dirty and full of bacteria, and is apt to disturb the stomach. It is largely psychical in effect and should not be overdone. During the next few days the bowels are kept open by mild laxatives, as compound licorice powder (one teaspoonful), or a tamarind pastille (Grillon), or an enema; one must avoid diarrhea, which disturbs rest.

The cough is an urgent indication, because it hinders clotting and thrombosis. Morphin muriate is especially suited to this purpose, because it also lowers the blood-pressure. The first dose should be given by the hypodermic method, in order to insure rapid action; subsequently in powder or drops up to 0.005 or 0.01 or 0.03, depending on the nature and the previous habits of the patient.

Reliable hemostatics we do not possess, but experience seems to show that some are of assistance, even if their mode of action is obscure. Noteworthy are:

℞.	Extr. sec. cornut. dialysat.		3.0
	Spir. dilut.		
	Glycerini		
	Aq. dest.	āā	5.0

M. Sig.—One injection every hour, until the bleeding stops; internally also if necessary.

(The ordinary extr. sec. cornut is too painful).

℞. Ergotin	1 0
Aq. dest.	10.0
Glycerini	5.0

Sig.—Ten to twenty drops every two hours.

℞. Ergotin	
Ac. tann.	āā 1.5
Extr op. aq.	0.05
Extr. liquir.	q. s.

Ut F. pil. No. 20.
Sig.—One pill every three hours.

These pills are particularly serviceable, and may be put in the hands of the patient for use in case of emergency.

Further, tannalbuminate, lead acetate (sacch. alb. 0.5, plumb. acet. 0.05, morph. mur. 0.005, every two hours), and iron sesquichlorid are used. An old tradition is the administration of a teaspoonful of common salt, which is supposed to irritate the gastric nerve, the vagus, and to set up reflex constriction of the pulmonary vessels.

The inhalation of 1 per cent. liq. ferri sesq., as recommended by von Ziemssen, will hardly meet with favor, since the forced breathing, even if it occurs at intervals of half an hour, hardly complies with the indication of rest.

Inf. digitalis, 1.5 : 150, has acted well in some cases of obstinate bleeding. In four cases in which other measures failed, I brought the bleeding to a sudden stop by inducing vomiting with an emetic. The effect may be similar to that of salt, namely, irritation of the vagus. It is only in exceptional cases, however, that an emetic is indicated.

An ancient hemostatic measure—tying off the extremities—has recently been revived by von Dusch, G. Seitz, and others. Bandages are applied to the middle of both thighs and arms tight enough to obstruct the venous return without interfering with the arterial influx. Thus a part of the blood is dammed up in the limbs, and the rest of the body becomes correspondingly depleted. In about one-fourth hour the bandages are gradually relaxed. The old custom of blood-letting is now out of date.

The hemorrhage is sometimes so severe that the blood rushes from the nose and mouth, the patient becomes cyanotic, and is threatened with choking from the blood and clots in the bronchi. Here the danger is from delay and rest is no longer the indication. One urges the patient to cough, gives champagne, and inserts the finger as far as possible down the throat, so as to remove the clots.

Cayley attempted to arrest a severe hemorrhage by inducing an artificial pneumothorax on the diseased side.

In hemoptysis, all warm, alcoholic, or carbonated drinks and all stimulating foods are to be excluded. Fluid diet is best. Cooled (but not ice-cold) milk, one-sixteenth of a liter, is taken every quarter of an hour, with the addition of an egg, powder of meat, eucasin, or nutrose. From this one proceeds to chopped meat and the ordinary diet, insisting only that everything is taken rather cool, and that alcohol is avoided.

The patient should remain in bed for a few days after a hemorrhage, or rather after the disappearance of the last traces of blood, since there is a tendency to recurrences in the next few days.

If certain authors permit the patient to get up very soon after or even during the hemorrhage, they may occasionally escape the penalty therefor; but I should strongly advise against such perilous experiments.

PAIN.

For pain, if occasioned by pleuritic irritation, we may use mustard plasters, Wlinski paper, tincture of iodin, or dry cupping; for the so-called rheumatic pains, neuralgias, and functional muscular tiredness, inunctions with linimentum volatile, veratrine salve, chloroform oil, or lard, the effect of which is chiefly due to the massage; or, finally, electricity. Moist, warm applications, linseed cataplasms, or hot-oil compresses, seem to be of service in both varieties of pain. Long strips of adhesive plaster, which fix the diseased part of the chest, or at least the seat of pain, work extremely well. For excessive hyperesthesias, especially in nervous patients, I have used Franklinization (electric breeze) with great success.

Internally we can give antifebrin (0.2), or phenacetin (0.5 to 1.0), or sod. salicyl (1 gm. three times a day); only in exceptional cases is a morphin injection to be called into requisition. The pains due to the traction of pleuritic adhesions are best combated by easy mountain-climbing, if the strength permits. I should not recommend the use of steam baths; one must always remember that pain is occasionally the precursor of hemorrhage.

DYSPNEA.

Dyspnea rarely demands relief. Its treatment, when due to dry or serous pleurisy, may be found in the corresponding part of this work. If it is due to stagnation of the secretions, light exercise and mountain-climbing, graduated to the general condition, are the best remedies. In asthmatic attacks potassium iodid with or without stimulating expectorants, senega, etc. (pot. iod. 5.0 : 150, or inf. senega 15 : 150, tinct. op. benz. 1.5), the thoracic compress, the inhalation of fumes of stramonium, incense-powders, asthma-cigarettes, and saltpetre paper often bring relief. Riess recommended pilocarpin. Pneumatic cabinets with compressed air, though of such marked value in typical bronchial asthma and other affections, are only exceptionally indicated in phthisis (see page 594). In any event, caution demands that consumptives be kept in separate cabinets.

If pressure of swollen glands upon the vagus is the probable cause of the dyspnea, we may use soft soap externally and potassium iodid internally.

Dyspnea resulting from diminution of the respiratory area by the destructive process, can be relieved only by reducing the demand for oxygen by absolute rest. In case of cardiac weakness, injections of camphor in oil are of temporary assistance (see page 581). If other means fail, especially in the advanced stages, morphin is indicated.

CARDIAC WEAKNESS.

Excitement of the heart may be calmed by an ice-bag or a Leiter's coil (a spiral coil of thin rubber, through which water runs). Winternitz recommends a moist pack of the whole body, until the circulation is somewhat reestablished, *i. e.*, for one-half to three-fourths of an hour, followed by a brief shower; this method can be employed, however, only in strong individuals.

Cardiac weakness demands rest and care, alternating perhaps with graduated exercises. The patient must avoid rapid or violent exercise; sudden death has been caused by getting up too quickly. For passing attacks we may give cognac or champagne in moderate doses, especially if there is a coincident fall of temperature; for continued weakness, the injections of camphor in oil, as recommended by Alexander, are particularly good (see page 581). Digitalis and strophanthus do not promise very great results in phthisis.

INSOMNIA.

Insomnia is a serious symptom; it produces not only physical but also mental depression. It may often be remedied by gradually extended sojourns in the open air, both night and day, by mental rest in the evening, by early supper, regulation of the bowels, and avoidance of sleep in the daytime. It is of importance to have a quiet and well-ventilated bedroom, in which the windows are always kept half or entirely open; draught is, of course, to be avoided. A glass of genuine Bavarian beer at night, Culmbacher, Siechen, or English porter, are often efficacious. Moist abdominal binders, or wet stockings which become heated in bed, or a glass of fresh water before retiring, are successful procedures.

If these measures fail, we may try a minimal constant current (0.5 to 1.0 milliamperes) to the forehead and neck, but cautiously, since otherwise it may intensify instead of improving the condition, as it at times does to a marked degree.

As a last resort, we turn to potassium bromid (1 to 3 gm.), paraldehyd, trional, sulfonal (1 to 2 gm. may be taken in an alcoholic drink, also useful for night-sweats), and the *ultimum refugium*, morphin.

DIGESTIVE DISTURBANCES.

Gastro-intestinal disturbance demands most careful attention, since a healthy digestion is our best ally and a necessary adjunct in the cure.

Nervous anorexia is combated by change of climate, the open-air cure, hydrotherapy, dietary methods, the use of stomachics, creosote, guaiacol and its carbonate, lavage, electricity, and, if there be anemia also, by the use of the mineral waters (Roncegno, Guberquelle, and Levico). I would only urge moderation in this matter of forced feeding, important as it is, so that the digestive organs do not become exhausted.

At the first signs of gastric disturbance the patient is put upon fluid diet for a few days, if his general condition permits, and limited to only the necessary amount of food; the deficiency can be made up by nutrient enemata (see page 537). The patient is put to bed and moist hot compresses are applied to the stomach.

For atony: restriction of fluids, frequent meals, eating slowly; scraped and chopped meats of all kinds, leguminous porridges; hydrotherapeutics. For fermentation, to improve the tone, massage, electricity, hydrotherapy (douche), creosote. ℞. Tr. strych. 3.0, tr. rhei vin., tr. valer., æth., āā 10.0; 20 drops three times a day before meals.

For gas and distention: menthol 2.0, sacch. alb., gummi arab., āā 1.5; ft. pil. No. 30. S.—One pill three times a day.

For pyrosis: magn., usta., natr. bicarb., āā 25.0; ½ to 1 teaspoonful three times a day, one-half hour after meals.

For hyperacidity: milk, which is at the same time a food and a chemical binder of the HCl, and especially Carlsbad salts.

For subacidity: HCl, HCl and pepsin, amara.

For anacidity: bitters, and semi-fluid diet, leguminous food, etc., little fat and meat, but eucasin, nutrose, etc.

For pain and nervous hyperesthesia, chloroform 1.0, bism. subn. 5.0 and 200; one dessertspoonful, three times daily, after shaking. Or, bism. subnit. 5.0, extr. conii 1.0 (or extr. belladon. 0.25), sap. q.s.; f.p. No. 100; three times a day one or two pills a.c.; or, according to Ewald, codein, phosph. 0.1, bism. subnit. 20.0, pulv. rhiz. calami, sacch. alb., āā 20; M.; f.p. Sig.—As much as will go on the tip of a knife. Plenty of meat, *i. e.*, albuminous food, and little of the carbohydrates. In nervous nausea the patients are given their meals in the recumbent posture, and maintain this for some time; in addition, the clothes, including the corset, should be loosened (Boas).

Vomiting: if due to cough and pharyngitis these are to be combated. The reflexes are to be deadened by potassium bromid. Also, orexinum basicum 0.3, in capsules or chocolate tablets, three times a day, one hour before eating; further, tinct. iod., chloroform, āā 5.0; 5 drops in water at meals, night and morning.

For constipation: defecation at a regular time; sour milk whey, fruit, compote, pumpernickel, cider, light white wines (Carlsbad water), tamarindien, rhubarb with magnesia, cascara sagrada in wine or in pastilles, oil enemas (Fleiner, Kussmaul), massage, electricity.

Five hundred cc., or in women 400 cc., of olive oil are allowed to run into the rectum within twenty to thirty minutes, the patient maintaining the dorsal or knee-chest position. The patient then lies with the pelvis elevated for about one-fourth of an hour, first on the right, then on the left side. It acts in four to five hours.

The diarrhea is either catarrhal, tuberculous, or amyloid in nature.

For dyspeptic and catarrhal diarrhea: first, cleansing of the gut with castor oil or calomel. Then gruels, acorn-cocoa (no coffee), almond-hempseed-milk, three-day kefir, wines rich in tannin, red wine (*e. g.*, Kamariter, Ott, Würzburg) very rich in tannin, huckleberry wine (*e. g.*, Fromm). Further, suitable both for tuberculous ulceration and also for amyloid degeneration, such food as leaves no great amount of solid residue, viz., little of vegetables and bread, and more of a fluid diet. For pain, applications, cataplasms, abdominal bandages, morphin subcutaneously, and chloral hydrate.

Favorite medicaments are:

Tannin 0.25, opii 0.025, several times a day; tannigen 0.5 to 1.0, three to four times a day; tannalbumin 1.0, and tannalbin 1.0 to 2.0, several times a day; plumb. acet. 0.03 with opii 0.01, several times a day.

Calc. phosph. 10.0, ac. tann. 1.0 (–2.0); div. in doses 20 to 10, four to six powders a day.

Cotoin 0.5, sacch. 5.0; div. in dos. 10, one powder every three hours.

Bism. sal., sacch. lact., āā 0.5 (opii 0.02). M. f.p. dos. 10. Sig.—One powder every two to five hours.

Decoct. rad. colombo (12 to 15.0) 120.0, tinct. opii simpl. 1.0, syr. aur. 30.0. Sig.—One teaspoonful every one to two hours.

For diarrhea due to tuberculous ulceration:

Ac. lact. 3.0, aq. dest. 100.0. M. Sig.—One teaspoonful three times a day.

Also rhatany and catechu. Liebermeister recommended zinc oxid 0.1 to 0.2 several times a day; Hérard, Cornil and Hanot, zinc oxid 3.5, sod. bicarb. 0.5. M.; f. p. div. in part. 4. Sig.—One powder a day. Further, enemata of silver nitrate 0.1 to 0.5 : 100 pro dosi, d. ad vitr. nitr., alternating with starch enemas with opium mucil. amyl. 100.0, tr. opii gtt. 10. Sig.—One enema.

For rectal fistula, the radical operation is indicated.

ANEMIA.

Anemia is to be combated by increasing the nutrition, and by the fresh-air treatment in combination with rest. In addition, we use the iron preparations, *e. g.*, ℞. ferr. lact., potass. iodid, āā 10.0, pulv. alth. q. s. ut f. pil. No. 100. Sig.—Two or three pills t. i. d., the iron-containing waters Levico, Guberquelle, Roncegno and also hemoglobin pastilles (Pfeuffer), according to the condition of the blood.

LARYNGEAL COMPLICATIONS.

For the hoarseness due to pressure paralysis we use electricity, and, in so far as swelling of the bronchial glands is at fault, inunction of the chest with soft soap, and potassium iodid internally. For hoarseness which appears and disappears several times in the day, I have sometimes found inhalations of potassium bromid serviceable.

An accompanying non-specific laryngitis requires the usual treatment (inhalations, etc.).

Tuberculous ulcers are treated by insufflations of iodol (Lublinski), sozoiodolzinc (1.0 to 2.0 : 10.0 of talcum), aristol, dermatol, tannin, ammonium bromid (Gerhardt), orthoform (anesthetic). Painting or gentle rubbing of the ulcers with lactic acid (30 to 80 per cent.) is of value, as was recognized by Heryng and Krause; it is done once or twice a day, or less often, according as the patient stands it. Deep ulcers require, in addition, curettement and electrolysis (Kafemann, Heryng). Severe edema demands scarification or incision, at need. Inhalations of the drugs previously mentioned often act well. For the rest, the ulcers occasionally heal spontaneously, and too energetic treatment is not desirable.

If severe pain and dysphagia interfere with the taking of food, morphin, codein, or opium is added to the insufflations, or the parts are painted several times a day with 30 to 50 per cent. antipyrin (M. Schmidt), or cocain (cocaini hydrochl. 0.5 to 1.0 to 2.0, aq. dest. 8.0, spir. 20. Sig.—For external use), or a combination of both (antipyrin 2.0, coc. mur. 1.0, aq. dest. 10.0, Wroblewski); unfortunately the effect is very evanescent. Menthol, introduced by A. Rosenberg, is of value. In addition to its anesthetic effect, it influences the tuberculous process very favorably. It is used for inhalation by means of the apparatus of Schreiber or Siemon, or in 20 per cent. solution in oil, for intralaryngeal or intratracheal injection, and for painting tuberculous ulcers of the larynx or trachea. The intralaryngeal application brings great relief in painful dysphagia, and since the anesthesia lasts about one-half to one hour and is not accompanied by any such disagreeable effects as is cocain, it permits the patient to take a large amount of food. The food should be fluid and semifluid and not too warm. Strongly spiced and acid food and concentrated alcohol are to be avoided.

Tuberculous ulcers of the pharynx require the same treatment.

In disease of the larynx, as of the lung, the chief point is to keep the organ at rest and protected from injurious influences. Speaking is excluded as far as possible and writing substituted.

Severe dyspnea occasionally demands tracheotomy. M. Schmidt recommended it, even in the absence of a vital indication, for rapidly progressive laryngeal disease, and especially for dysphagia, in case other remedies were without success; he has found few followers.

OTHER MEASURES.

We must also have an eye to the occupation of the consumptive during the period of enforced idleness. This has already been indicated in connection with the rest cure. Prolonged inactivity is harmful in many ways. Like other men, the consumptive develops the habit of slothfulness, and becomes unfitted for regular employment. As he improves, he should be gradually broken in to work again. The ennui, which might be regarded as a favorable indication of mental rest, serves to spur him on to all sorts of useless pranks, and so, indirectly, interferes with the regular progress of the cure.

His usual pleasures and avocations are not to be interfered with, unless they are injurious. For instance, it is unnecessary to cut off smoking entirely; this is indicated only for affections of the neck and throat which are aggravated by the irritation. Otherwise, a good cigar after dinner or supper does no harm, and often improves the appetite and digestion if the patient is accustomed to it. At the first sign of irritation, smoking is, of cours , to be forbidden. The inhalation of smoke, and also the use of cigarettes, is absolutely prohibited.

In sexual matters the consumptive must observe absolute abstinence as long as the process continues to progress. With the return of strength and well-being, however, a strict compliance with this demand becomes irksome to the patient, and it is best, then, to permit indulgence within definite limits.

On the other hand, we should never permit the patient to marry as long as the disease progresses; in young people death is almost invariably the result. But after there has been a relative recovery, when the *symptoms* have been in *abeyance* for *two or three years* and the patient maintains a satisfactory general condition, I believe that we have no right to forbid marriage. If a man is fairly well-to-do and if his wife makes no very severe demands upon him, he ordinarily has far more comfort and rest and better care in the married state than as a bachelor, not to mention all the dangers of single life—gonorrhea, syphilis, etc. On the other hand, a woman may be seriously harmed by marriage with all its consequences, especially the puerperium, unless she has been thoroughly toned up. For the sake of the offspring, permission to marry should be withheld not only until the patient has made a relative recovery, but until the general condition is satisfactory. I have seen a number of such marriages give origin to many children, who were perfectly strong and well developed. I should consider it wrong in such cases to forbid marriage. We must, therefore, conscientiously decide whether conditions justify us in forbidding to our patient any of the pleasures he might enjoy during his brief life; the matter should be viewed from a practical standpoint.

In consumptive women conception is to be strongly discouraged, since they stand the puerperium badly. The disease often assumes its most acute form after childbirth and proves rapidly fatal. In such cases perfect frankness toward the fiancé is to be recommended. In far-advanced cases, when pregnancy means almost certain death, it is morally justifiable to sacrifice the doubtful chances of a puny infant to the imperiled existence of the mother by inducing an early abortion. This decision is to be embraced, of course, only on the basis of a mature experience, and after careful and earnest thought. For instance, eight years ago I was asked by one of our most prominent gynecologists whether a consumptive who had been in my care was able, in view of her pulmonary condition, to stand the approaching puerperium. I gave a tentative answer in the affirmative. I saw the mother and the child five years later, and the former had even improved.

On the other hand, two years ago I treated a phthisical young woman who had been ill about one year before, but in whom the marked gain in flesh and the gradual disappearance of the objective symptoms seemed to indicate an approaching cure. She conceived, became the victim of uncontrollable vomiting, and lost over twenty pounds within the first two or three months of her pregnancy; she lost ground visibly, and the objective signs daily became more marked. Reasoning that vomiting may continue until the delivery even in the first pregnancy, and that tuberculosis may then evince its power, I had no doubt that the patient was doomed to a swift and sure death—perhaps even before the pregnancy should have been completed. After careful deliberation, therefore, I believed that it was incumbent on me to induce abortion; this operation was, in fact, followed by relatively rapid recovery.

I have already stated that a sick mother should not nurse her child.

MANAGEMENT AFTER RELATIVE CURE.

When the process has happily been quiescent for a considerable time, when all the subjective disturbances have disappeared, and the physical examination gives evidence of cicatrization, of induration, or of a dry cavity, the patient should still continue to observe caution in his mode of life. He must avoid immoderate physical and mental exertion, and all excesses in *Baccho et Venere.* Years later, for example, violent exercise (as in sport) may give rise to fatal hemorrhage from an aneurism in some old cavity. We should insist that the day's work be broken by intervals of rest, that there be sufficient time for sleep, that the home be healthful and light and not too far away from the place of business, and that there be ample opportunity for sojourn in the fresh air. If feasible, the patient should give up an occupation which is injurious, and should live in some healthy city (in Germany, *e. g.*, Wiesbaden or Freiburg i. B., certain Thuringian cities, or certain suburbs of Berlin).

The weight should be taken every four weeks, and if there is any sign of discomfort or of weakness, the temperature should be immediately taken. If there is steady loss of weight with elevation of temperature, or night-sweats, expectoration, and hemoptysis, the physician should be immediately consulted. Every disease, especially those of the respiratory tract, is to be regarded as of importance. Such continuous watchfulness renders it possible to forestall every recurrence at its very inception.

ACUTE GENERAL MILIARY TUBERCULOSIS.

ACUTE GENERAL MILIARY TUBERCULOSIS.

INTRODUCTION.

The term "miliary tuberculosis" is applied to the appearance of numerous small, gray or grayish-red tuberculous nodules about the size of a millet-seed and approximately at the same degree of development in an organ, especially the lung, or in only a certain portion of the lung. The characteristics of the tubercle, its production by the bacillus, the histologic structure and various stages of development have been described in detail on page 89 of this work.

By general miliary tuberculosis we designate the fairly regular distribution of such nodules in all or several of the organs of the body, particularly the lung, liver, spleen, kidney, brain, bone-marrow, etc. As a rule, the disease is acute and is characterized by a tumultuous course, terminating in death usually in a few weeks (acute general miliary tuberculosis). This variety forms a separate, well-marked clinical picture, and therefore requires a special description.

There are no trustworthy statements in the literature in regard to the frequency of miliary tuberculosis. It occurs at all ages, from earliest childhood to extreme age, but is distinctly more common in the early, formative years and not infrequently attacks apparently healthy individuals. Most of the children are from one to four years old; the youngest child affected with miliary tuberculosis observed by Demme was seven weeks old.

CHAPTER I.

ETIOLOGY.

PREDISPOSING CAUSES OF MILIARY TUBERCULOSIS.

There are four prominent factors in the etiology of acute general miliary tuberculosis.

The development of tubercles in organs that have no communication with the outside whatever, such as the spleen and kidney, cannot be explained by direct infection from without, and must therefore begin within the body, in a preexisting or, in other words, an old, possibly latent tuberculous focus. The fact that all the miliary tubercles, or at least certain groups of them, are approximately at the same stage of development, indicates that the deposition of infectious material in the tissues takes place all at once or practically at the same time.

This simultaneous deposition of tubercle bacilli in the various organs, especially those which have no communication with the outside, is conceivable only by way of the blood-channels, which is the only medium capable of supplying the most distant and various organs with tubercle bacilli practically at the same instant. In animals, also, typical general miliary tuberculosis, characterized by the presence of tubercles at the same stage of development in all organs, can only be imitated by intravenous injection, that is, by blood infection.

Conversely, as Baumgarten has demonstrated, blood taken from animals suffering from inoculation tuberculosis of a severe type when inoculated into the anterior chamber produces a typical tuberculosis. In man Weichselbaum, Meisels, Lustig, Rütimeyer, Sticker, and others later found tubercle bacilli in the blood.

Finally, the enormous number of tubercles produced indicates that the blood-channels are invaded by an overwhelming mass of tubercle bacilli.

It is evident, therefore, that an old focus and the entrance of numerous bacilli into the blood-channels are necessary prerequisites for the occurrence of acute general tuberculosis.

The frequent coincidence of large tuberculous foci in a state of cheesy degeneration that have existed for some time with miliary tuberculosis attracted the attention of so early an observer as Laennec, who did not fail to recognize the intimate connection between the two conditions. But their mutual relations were not accurately determined until 1856, or rather 1858, by Buhl. Differing from the views of his predecessors, this author did not regard miliary tuberculosis as the last link in the chain of an already existing disease, but declared it to be a specific disease due to absorption and infection that always owed its development to the presence of a tuberculous, or cheesy and purulent, infectious focus. When the constituents of such a cheesy focus are absorbed by the blood- or lymph-vessels, the multiple development of tubercles (autoinfection) is the result.

This doctrine of Buhl's contributed greatly to a clear understanding of the origin of miliary tuberculosis, besides supplying the strongest impetus to the subsequent elaboration of the infection theory of tuberculosis.

But the supposed preexistence of a former focus does not quite explain everything. In the first place, the presence of old tuberculous foci cannot always be demonstrated, although the number of cases in which they are not found is very small. Buhl failed to find them in only 8 to 10 per cent. of his cases, and later observers in even fewer. This, however, is not difficult to explain; for a focus of this kind may be exceedingly small and escape even the most painstaking examination, and yet be quite sufficient to produce an infection. We know that in man very small tuberculous foci may be hidden even in apparently healthy glands which show practically no signs of change (Pizzini, Cornet, Spengler, see page 226). In a case of widespread generalized tuberculosis in a guinea-pig I once found that the lymph-gland nearest the point of infection, although scarcely enlarged, was studded with softened foci about the size of a pinhead, containing tubercle bacilli—such a gland, in fact, as would certainly have been overlooked in the human cadaver. Failure to find a focus is therefore no proof of its non-existence.

On the other hand, it is more difficult to explain why, in spite of the existence of such caseous foci, infection of the entire body is the exception. It was quite properly objected to Buhl's doctrine that, as Engel had pointed out, the very cases in which the most extensive tuberculous foci are present—for example, widespread pulmonary tuberculosis—very frequently fail to develop a miliary tuberculosis; while, on the other hand, small foci are quite often associated with miliary tuberculosis. Buhl tried to meet this objection by formulating another requirement, namely, that the primary cheesy focus must not be completely encapsulated, not surrounded on every side by fibroid tissue so that absorption and infection may take place more readily; but even when these conditions are fulfilled, a local miliary tuberculosis may develop at the periphery of the focus, but not always actual general miliary tuberculosis.

The presence of an old cheesy focus in itself, then, does not satisfy all the prerequisites for the development of general miliary tuberculosis; certain other incidental factors are also necessary. What these factors are, how the tuberculous poison or the tubercle bacilli, which were not known in that day, find their way into the blood-channels—these questions found no answer until Weigert, by discovering tuberculosis of blood-vessels, threw additional light on the subject.

Whereas the belief formerly prevailed that the intima of large vessels was immune against tuberculosis (Rokitansky), Weigert in 1877 discovered tuberculosis in patulous veins still capable of functionating (especially in the larger veins of the lungs). This discovery led him to seek the origin of miliary tuberculosis in tuberculosis of the blood-vessels, and he, in fact, succeeded in defining with extraordinary precision all the points in the mechanism of its production—an achievement that derives additional lustre from the fact that the tubercle bacillus and its biologic peculiarities were unknown at that time. As a matter of fact, once attention had been called to the point, vascular tubercles of this character were found in a number of cases of acute miliary tuberculosis.

Tubercles were found in veins also by the following observers besides Weigert: Mügge, Schuchardt, Weichselbaum, Bergkammer, Hanau, Hauser, Meyer, Will, Heller, Brasch, Banti, Schmorl and Kockel, Sigg, Benda, and others.

Shortly after Weigert's first discoveries Mügge, the disciple of Orth, had established the occurrence of tuberculosis in the arteries of the lungs, and after him Marchand, Weigert, and later Cornil (in the small vessels of the brain), Schuchardt, Dittrich, Benda and others also found tubercles in arteries.

In addition, tuberculosis of the thoracic duct, which was discovered even before Weigert's time by Ponfick, who in turn had a predecessor in the person of Astley Cooper (1798), indicates a channel by which degenerated bacilli may reach the general blood-path indirectly, namely, through the subclavian vein, and thus be scattered broadcast through all the organs. Tubercles have also been found in the thoracic duct by Weigert, Koch, Meisels, Brasch, Hanau, Sigg, and Benda.

CAUSAL RELATIONSHIP BETWEEN TUBERCULOSIS OF BLOOD-VESSELS AND MILIARY TUBERCULOSIS.

The intimate etiologic relations between this blood-vessel tuberculosis and acute general miliary tuberculosis are at once suggested by the limited occurrence of these vascular tubercles. So far they have been found only in connection with miliary tuberculosis, in which disease, however, they are exceedingly common. In addition, their size and extreme degree of caseation indicate that they are older in development than the disseminated miliary tubercles.

It appears from Hanau-Sigg's analysis that, up to 1896, 102 cases of general miliary tuberculosis were explained in this way—70.8 per cent. of Weigert's, 65.1 per cent. of Hanau's, and 82.8 per cent. of Sigg's cases. It is not surprising that the blood-vessel foci have not been found in every case; for it is practically impossible to open all the vessels, and the examination requires a good deal of practice. The degeneration of these blood-vessel tubercles fulfils all the conditions that have been mentioned as necessary for the production of miliary tuberculosis. Tubercle bacilli—in the case of a large focus, innumerable bacilli—probably collected into small masses, plugs, or fragments, entering the blood-stream all at once, are uniformly and widely distributed by the latter. When they are derived from an arterial focus, the bacilli are carried into the corresponding organs; but when they emanate from a focus in a vein or in the thoracic duct, they are carried into the general circulation and reach all the organs of the body.

Whether in a given case a blood-vessel tubercle found in a cadaver may actually be regarded as the origin of an existing acute miliary tuberculosis is another question.

Weigert made it a condition that, among other things, the blood-vessel tubercle must be older in structure than the acute miliary nodules, that it must be situated in a patulous and not in an obliterated vascular channel and must account for the escape of a sufficient quantity of poison (bacilli), and that the poison (bacilli) must, as a matter of fact, have reached the surface of the blood-vessel focus.

These conditions are no doubt correct so far as the time when an acute miliary tuberculosis begins is concerned; but it can hardly be expected that they will be found to have been complied with in the cadaver, because in the interval between the beginning of the disease and death the focus may have undergone many changes. For example, the ulcerated focus from which tubercle bacilli in large quantities have been distributed may have become covered with fibrin coagula and shut off from the general circulation. Thus it is not uncommon, on examining one of these blood-vessel foci, to find within a cheesy mass that contains the bacilli, irregular ragged openings filled with fibrin deposits which make the surface appear perfectly smooth and simulate an intact tubercle (Benda). A smooth shining surface therefore does not preclude the former existence of an ulcer, and the objection raised by Ribbert and Wild that the disease is directly derived from a vein tubercle only in exceptional cases, on the ground that ulceration is frequently absent, is not valid.

On the contrary, I am inclined to believe that the finding of ulcers and a slightly roughened and somewhat opaque surface quite often indicates not a focus of weeks' or months' standing, but a lesion produced immediately before death, an ante-mortem relapse having no relation whatever to the general tubercle formation. The occurrence of stratified deposits of fibrin (Benda) rather suggests that ulceration may take place repeatedly within the focus. At death it is quite possible that the entire vascular area that is the seat of the peccant tuberculous ulcer may be thrombosed and obliterated.

It is to be remembered also that even the entrance of masses of bacilli into the blood-channel does not by any means necessitate the presence of a large perforation, plainly visible to the naked eye, which some authors believe to be necessary. This will be appreciated by remembering the size of the bacilli. An ulcer only 0.1 square millimeter in size, which ordinarily would not be recognizable with the naked eye, would permit the passage at the same time—that is, in parallel and superimposed ranks—of more than 100,000 bacilli.

The number of bacilli found at an autopsy is of no significance so far as the etiological relationship between a blood-vessel focus and miliary tuberculosis is concerned. In many of these blood-vessel foci the bacilli are extremely numerous (Hauser, Kossel, Hanau). In most of his blood-vessel tubercles Benda found "quite extraordinarily abundant accumulations of tubercle bacilli," which on staining become distinctly visible to the naked eye. While, then, an abundant dissemination of bacilli is readily explained in such cases, it is not excluded in those cases in which only occasional bacilli are found; for it is quite possible that the blood in its onward movement may have washed away the softened infectious masses lying free in the channel.

As regards the number of bacilli necessary for the production of an acute miliary tuberculosis, many authors who speak of billions are guilty of the wildest exaggeration. Since only one billion of tuberculous nodules about ⅛ of a cubic centimeter in size (which is not very large) would take up a space equivalent to 125 liters, although the entire body of an adult man is equivalent in capacity to only 70 liters, what would become of skin, bone, muscle, and brain? Some regard for the mathematics of a proposition should be observed in medicine.

In the superficial layers of the blood-vessel tubercles bacilli occur practically in pure cultures (Hanau, Benda, and others). In these cheesy fragments about ¼ of a cubic millimeter in size there may be more than one million bacilli 0.0015 mm. long and 0.0003 mm. thick, which, on a modest estimate, is quite enough to produce a miliary tuberculosis in all the organs of the body. The fact that a blood-vessel focus in the cadaver is not ulcerated and contains but few bacilli in nowise militates against its significance for the production of miliary tuberculosis.

DO THE TUBERCLE BACILLI MULTIPLY IN THE BLOOD?

Any other explanation of the sudden flooding of the blood with bacilli than by the entrance or rupture into the blood-vessels of the bacilli in large quantities is hardly conceivable. The attempt has been made to explain the great number of bacilli by assuming that they multiply within the blood itself. According to Wild, only small quantities succeed in reaching the blood; part of these are deposited in the organs, where the bacilli proliferate and then secondarily flood the blood with germs, while the other portion multiplies within the blood itself, providing favorable conditions are present for their development, until a number sufficient to cause an acute general miliary tuberculosis is reached. When the conditions are unfavorable, they are rapidly eliminated from the body without leaving a trace.

This hypothesis seems to me absolutely untenable. In the first place, Wild's assumption is exceedingly forced. That author professes to believe that the predisposition, which the phthisical subject manifests clearly enough in the extensive tuberculous foci and in the miliary tuberculosis at the periphery of these foci and finally confirms by his death, does not suffice for the development of generalized miliary tuberculosis, and that, in addition to a "moderate degree" of predisposition present in pulmonary phthisis, a "much greater" predisposition is necessary for miliary tuberculosis.

This assumed occasional innocuousness of tubercle bacilli in the phthisical body is not by any means proved by Jani's investigations, to which Wild makes appeals for confirmation; for although the latter found tubercle bacilli in the healthy testicles of phthisical cadavers unaccompanied by any pathological tissue changes in the surroundings or elsewhere in the affected organ, it is none the less true that (1) Jani failed to prove that the bacilli are virulent; and (2) if we admit that the bacilli were alive, there is a much simpler explanation for the absence of any signs of reaction. Elsewhere (see page 451) I pointed out that microscopic tubercles or bacilli are not infrequently found not only in the testicles, but also in the various other organs of phthisical cadavers, if they are specially looked for. Brissaud, Toupet, Arnold, almost regularly found such microscopic foci, and Jani's findings in the testicles belong to the same category. The failure of miliary tuberculosis to develop in such cases is evidently not due to the fact that the phthisical subject was not sufficiently predisposed, but solely to the fact that the body, which is already overloaded with tuberculin, succumbs to the toxic influence when an additional mass of living and dead bacilli are poured into the blood-channels before reaction can take place, just as tuberculous animals are killed even by small doses of tuberculin.

Besides all this, it is pure speculation to assume that bacilli frequently circulate in the blood of phthisical subjects; for the actual finding of the bacilli in the blood has never been demonstrated beyond the possibility of a doubt, except in acute miliary tuberculosis, and exceptionally during the last moments of life in phthisical patients; and in the latter instance their finding indicated not a harmless circulation, but rather the precursor and immediate cause of death. If, however, they do not occur in the blood even in widespread phthisis, how much less likely are they to be present in the case of those small tuberculous foci which usually form the starting-point of miliary tubercles?

In the same way the theory that the tubercle bacilli multiply in the blood is purely speculative. We know positively that tubercle bacilli practically do not develop in fluid media, where they show their hydrophobic propensities by multiplying only on the surface and at the edges—in fact, mere wetting of the bacillus inhibits or retards their growth. Is it right simply to ignore this biological fact? The experiments of Wyssokowitsch, who found that pathogenic bacteria when introduced into the blood disappear altogether or in part in the circulation, are deposited in the internal organs, there multiply, and are again rapidly taken up by the blood, are quite incorrectly applied by Wild to the tubercle bacillus, for Wyssokowitsch experimented with bacteria capable of growing in fluid media and in the blood; for example, with the bacillus of anthrax. The tubercle bacillus is not a blood bacterium and does not grow in the blood, especially in the circulating blood, which is in constant motion.

The assumption that bacilli first enter the blood in small numbers and there undergo multiplication is thus not proved. In order to produce general miliary tuberculosis a simultaneous or practically simultaneous invasion of a large number of bacilli is necessary, such as is possible in cases of Weigert's tuberculous foci in veins and in the thoracic duct and, as will be seen later, under certain other conditions.

PATHOGENESIS OF BLOOD-VESSEL TUBERCLES.

The blood-vessel tubercle, which is such an important factor in the production of acute miliary tuberculosis, may be produced in one of two ways. The tubercle bacilli may enter the blood-vessel wall from a focus situated in the periphery of a blood-vessel, either in the natural course of their growth or through the lymph-vessels; or bacilli already contained in the circulating blood may be directly deposited on the vessel wall or may reach the vessel wall through the vasa vasorum. When a tuberculous focus by peripheral extension approaches a blood-vessel, the diffusible tuberculous poisons first reach the vessel wall, as was explained elsewhere in this volume, and cause irritation, inflammation, and thickening, after which they penetrate the wall and produce thrombosis or obliteration of small vessels both arterial and venous, so that the blood-vessel ceases to exist as such and cannot take any further part in the distribution of the bacilli. In the case of larger blood-vessels also the bacterial poisons cause thickening of the wall, but are unable at first to arrest the powerful current of blood. The thickened walls of the arteries at least usually offer sufficient resistance to the advancing tubercle bacilli, so that while the surrounding tissue undergoes degeneration, the artery preserves its integrity and power of functionating and passes across the center of the cavity, often undergoing aneurysmal dilatation under the strain of the blood-pressure. Later an erosion may take place either as the result of a tuberculous process or the great rise in blood-pressure, and may bring on a dangerous or even a fatal hemorrhage. But even in such a case there is but little danger of subsequent spread of the bacilli, as they are washed away from the lumen by the hemorrhage.

The processes in the walls of veins are similar, except that, owing to their more delicate structure, thrombosis and obliteration are effected much more easily and earlier in the course of the disease. If thrombosis is delayed, an occasional bacillus may make its way into the circulation. Thrombosis is the rule. Sometimes, however, especially in the case of larger vessels, the bacilli grow directly into the vessel wall and there establish a focus. The newly formed focus causes bulging of the intima; later it softens and breaks down, and pours out bacilli into the circulation. Finally it may be covered with fibrin to the extent of completely obliterating the vessel. For reasons given above, this process takes place more frequently in veins than in arteries, but well-authenticated cases occurring in the latter are also found in literature (Dittrich).

In quite a similar manner a peripheral focus may encroach upon the thoracic duct, break down in that situation, and thus produce the blood infection.

Even in the absence of continuous connection between a caseous focus and a blood-vessel wall it is possible for the bacilli to traverse a short stretch of tissue uninterrupted by a lymph-gland, reach the blood-vessel, and work their way through the wall.

A blood-vessel tubercle may also be formed through the agency of the circulation. If tubercle bacilli are already present in the circulating blood, they may become deposited on the wall, especially in small veins in which the circulation is slower, and multiply on the intima; or they may enter the vasa vasorum with the infected blood and there deposit themselves on the blood-vessel wall.

The blood-vessel tubercle in a given case is therefore not necessarily the source of an existing acute miliary tuberculosis, as both conditions may have a common origin, a previous flooding of the blood with bacilli, and therefore represent two coordinate conditions.

In the case of the thoracic duct the rôle of the blood is of course assumed by lymph and the blood is of importance only through the vasa vasorum. In this case the afferent lymph-vessels of the peritoneum and of the pleura are the most important (Brasch), because they are not interrupted by lymph-glands, which act as filters. Thoracic duct tuberculosis would perhaps be a more frequent condition were it not that the bacilli are arrested, especially in the recess called by Weigert the "Schlammfänge" (mud trap) and, as they enter the lymph-clefts, block their own passage through the irritation they set up in the walls.

The question as to which of these two modes of production is the most frequent in the case of blood-vessel tuberculosis has recently been made the subject of discussion by Ribbert and especially by Benda.

In Weigert's cases isolated cheesy nodules in the neighborhood of veins extended as far as the outer surface of the wall; others had worked their way through the wall and already produced delicate accumulations of cells on the wall; others, again, were beginning to encroach upon the lumen. In more advanced cases the bacillus had entered the jugular vein from the cheesy glands, which were densely adherent to the blood-vessel, and had set up a miliary tuberculosis in the adjoining muscles of the neck. Even in those cases in which a layer of sound tissue intervened between cheesy glands and the infected wall of the vein it was still possible to demonstrate—in one case by serial sections—a direct connection between the cheesy center of a vein tubercle and the cheesy extravascular focus, a small lymph-gland the size of a pinhead, such as Arnold had described in the lungs. Weigert accordingly attributes blood-vessel tuberculosis to erosion by an extravascular caseous focus and regards it as a true primary site of invasion. Similar pictures were obtained by Hanau and others, who agree with Weigert's interpretation.

Benda, on the other hand, believes that the mode of origin described by Weigert is rare, and that blood-vessel tuberculosis grows from within, having its origin in the blood, since occasionally the bacilli enter the blood- and lymph stream even in the absence of any coarse lesion—a theory erected in their time by Ponfick and Mügge to explain the origin of a miliary tubercle on the intima of the thoracic duct and of blood-vessels. Benda regards them as solitary or metastatic growths in the intima of blood-vessels, a tuberculous endangitis and not a tuberculous periangitis, that is, blood-vessel tuberculosis produced after the manner assumed by Weigert. He thought he found a support for his view in the transitional conditions from disease affecting the intima exclusively to that involving the outer blood-vessel wall also; in the fact that extravascular caseous foci adherent to the vessel wall are frequently not found in spite of the existence of extensive proliferation in the lumen; in the sudden appearance of recent foci derived from the primary focus, particularly in tuberculosis of the thoracic duct; in the appearance of multiple foci when it is hardly possible to assume a fresh rupture for each crop; and, finally, in the fact that the intima is not involved in cases of true rupture, as, for example, in those of Huguenin, which will be mentioned later.

Which of the two modes of origin is the more common it is impossible to decide in a general way. There is no doubt that both occur. When the blood-vessel tubercle is adjacent to a large perivascular focus, the origin of the former cannot well be conceived of in any other way than according to Weigert's theory, that is, as secondary to an extravascular focus; for it is most improbable that a focus produced in the lumen should break through the vessel wall, which forms a kind of barrier, when it has an open blood-channel at its disposal for further growth.

On the other hand, when there is no such connection and the extravascular focus is very small, and similarly when the blood-vessel foci are very numerous the development through blood infection from the blood-vessel lumen after Benda's theory seems more probable. The latter removes the ultimate etiology a step further, for the question why and whence the bacilli have entered the circulation still remains to be answered, and recourse must be had to a perhaps unrecognizable focus in Weigert's sense existing in an already thrombosed vessel.

Conversely, in the case of a Weigert blood-vessel tubercle in an organ that does not communicate with the outside, as, for example, the suprarenal vein, the ultimate origin of the contiguous renal tubercle must be interpreted according to Benda's theory. Both theories will therefore frequently be called into requisition to explain the same case. The etiology of a case of miliary tuberculosis cannot be regarded as satisfactorily explained unless the entire path of infection from without to the original cheesy focus, and from that point to a large rupture in the blood-vessel, can be traced in the cadaver.

OTHER MODES OF IRRUPTION INTO THE CIRCULATION.

Blood-vessel tubercles do not represent the only possible means by which large masses of bacilli can reach the circulation all at once. Sometimes, although apparently quite rarely, a true irruption, not preceded by the formation of tubercles, takes place instead of the tubercles working their way gradually into the blood-vessel wall. Examples of the first kind were observed by Huguenin in 1876, even before Weigert's discovery. In a case of miliary tuberculosis he found a lateral erosion in the pulmonary vein communicating with an empty cavity about the size of a bean. When the contiguous cavity is closed and does not communicate with the bronchus, tuberculous masses in the blood-vessel that has been opened in this way may be completely washed out into the circulation and thus be disseminated over the entire body. Similar cases were later described by Hanau (rupture of a pulmonary cavity into the aorta; the encroachment of a cheesy node on the pulmonary vein), and again by Huguenin and others.

Another path by which abundant masses of bacilli may reach the circulation was first observed by Koch. He found in the body of a man who had died of miliary tuberculosis, within the bronchial gland, which was swollen at the center, and in the immediate neighborhood of a few small arteries, such an enormous accumulation of bacilli that the vessel appeared to be surrounded by a blue areola. In some cases the bacilli had advanced to the lumen of the vessel.

Whether in this case the general miliary tuberculosis, which included the kidney, etc., really had its origin in small arteries which at first deposited the bacilli only in the area of their distribution, or whether there was, in addition, some other rupture, is impossible to decide.

In the case of a child that had died of miliary tuberculosis Bergkammer observed a similar bacillary areola surrounding blood-vessels, both veins and arteries, within the cheesy bronchial glands, and also accumulations of tubercle bacilli within the lumen. In a large patulous pulmonary artery, immured in cheesy bronchial glands, Weigert found abundant bacilli within the outermost cells, in the intervals between the cells of the pulmonary artery, and extending almost to the lumen of the vessels. Baumgarten also saw several parallel cases, as did Ribbert in chicken tuberculosis.

As regards the area where irruption is most common, the veins in this respect, especially the pulmonary veins, appear to be more important even than the thoracic duct. This is probably due to the tenuity of the venous walls and the slower movement of the blood. This relation has not as yet, however, been firmly established; for the figures are too small and the results show subjective variations depending on the particular region chiefly selected by the anatomist for his observations. While in 13 cases Weigert found the pulmonary vein affected eight times and the thoracic duct three times, Benda, of a total of 19 cases, allots 12 to the thoracic duct and only 4 to the pulmonary veins. As has been said elsewhere, the impression is irresistible that in many cases the condition, that which is regarded as the actual irruption, has nothing whatever to do with the existing miliary tuberculosis, the true focus having its seat in a vein which had long before become obliterated and unrecognizable. The impression is strengthened by the observation of various authors, especially Hanau, that quite frequently (in one-fifth of the cases) "more than one complete irruption, or, in addition to one or several complete irruptions, one that is not complete has been found." Sigg in one case found 15, Benda in another 14 foci.

In addition to the pulmonary veins and the thoracic duct, the vessels in which irruption has been established thus far are—the vena azygos, from the retroperitoneal glands (Klebs); the external jugular vein, also from a gland (Schuchardt); the internal jugular vein, from a gland (large, slit-like perforation, more than 1 cm. in width [Kaufmann]); the right transverse sinus, from carious bone (Hanau, Meyer, Will, Banti); the thyroid vein (Weigert); the innominate vein (Heller); the renal vein (Hanau); the suprarenal vein (Weigert, Hanau, Sigg, Eichhorst); the genito-vesical plexus (Weichselbaum); the heart (Lueken in 1865 and Schürrhoff); the aorta (P. Dittrich, Sigg); an open pulmonary artery (Herxheimer); and other small arteries or veins in the bronchial gland (Koch, Bergkammer, Weigert).

In other cases the starting-point is found in tuberculous foci in bones or joints; in tuberculosis of the intestines or mesentery, especially in children but also in adults (Zinn); in uterine or tubal tuberculosis (six weeks after delivery—Frankenburger, Weichselbaum); in lupus (Demme, cribriform perforation of the venous wall); or in any other cheesy focus that has existed for some time in any portion of the body, even although it is impossible to demonstrate what portion of the body has been affected or although no attempt has been made to do so. The prominent position occupied by the bronchial glands is emphasized by Abelin's observations, who noted that they were always profoundly involved in cases of miliary tuberculosis occurring in children.

EFFECTS OF THE IRRUPTION.

The effects of the rupture or irruption into the circulation in one of the above-described ways vary according to the number of the bacilli and the situation and character of the affected vessel.

In acute general miliary tuberculosis the blood is flooded with large numbers of bacilli, usually derived from larger foci, and the bacilli are carried into the veins or into the thoracic duct. The bacilli enter the right heart and deposit themselves at first and chiefly in the lung. A certain proportion of the entire number passes through the capillary system into the left heart and thence reaches the remaining organs, especially the brain, spleen, bone-marrow, choroid, kidney, etc., and in part also the serous membranes and the vessels themselves.

If rupture takes place into the pulmonary vein, the infection spreads chiefly to the organs supplied by the greater circulation.

After rupture into the distribution of the portal vein, most of the bacilli are arrested in the liver; a small remainder may enter the liver veins and thence reach the lung. If rupture takes place in the endocardium or in the initial portions of the aorta, in either case all the organs of the body are affected.

In cases of rupture in smaller arterial trunks the organs supplied by them are chiefly involved.

When only a few bacilli enter the blood, the miliary tubercles produced in the affected organs or in the entire organism do not suffice to bring on the death of the individual at once. The individual foci may therefore under certain circumstances attain considerable size. Isolated bacilli, such as often enter the circulation before the vessel has become completely obliterated, give rise to the so-called solitary tuberculosis.

When the bacilli enter the blood in repeated crops, as happens especially in children, a variable number of these tuberculous foci will be found in various organs, in various stages of development, and of different sizes. The picture of chronic miliary tuberculosis is produced, in which the frequency of the irruptions in a sense makes up for the small number of the bacilli. It may be combined with a secondary acute and copious irruption, and thereby bring about a sudden termination.

EXCITING CAUSES.

Why a miliary tuberculosis takes place at a certain time, and why it occurs from an old focus now in one situation and now in another, are questions that we are unable to answer. It probably depends mainly on the stage of development of the blood-vessel tubercle or of the perivascular focus. It is significant that in pulmonary tuberculosis, in which the cheesy foci attain their greatest size and produce the greatest amount of destruction, termination by miliary tuberculosis is apparently not the rule. This appears to indicate that the rupture into a vein is not a part of the normal development of tuberculosis.

There is a great difference of opinion in regard to the frequency of the combination of phthisis with general miliary tuberculosis. According to Ruehle, pulmonary tuberculosis is "one of the commonest causes of the production of acute miliary tuberculosis." Orth determined its presence in more than one-half of all cases, and Litten in 28 out of 52 cases of miliary tuberculosis found unilateral or bilateral phthisis present at the same time. Weigert found 18 cases of acute general miliary tuberculosis, or 3 per cent., among 600 autopsies of phthisical patients; and among 28 cases of acute miliary tuberculosis he found 10 without any changes in the lungs. The explanation of these discrepancies is that the statistics are based on too small a number of cases to be utilized for the purpose.

This much at least is certain—phthisis plays a tolerably important part in the etiology of miliary tuberculosis, while, on the other hand, acute general miliary tuberculosis with the development of tubercles (see page 634) is comparatively infrequent as a terminal manifestation of phthisis.

The reasons why acute general miliary tuberculosis is apparently rare in pulmonary phthisis are in part disclosed by a careful analysis of the causes which are responsible for the greater rarity of miliary tuberculosis in later life as compared with childhood.

When a tuberculous focus is formed in any organ of a child's body, the bacterial poisons or proteins, owing to the fact that the lymph-channels are broader and more permeable, are more readily diffused into the surrounding tissues. They reach the blood-vessels more rapidly, have less difficulty in making their way through the walls, which are softer in childhood, and, on the other hand, are taken up by the more rapidly circulating blood and carried on without leaving behind any material local irritation. The blood-vessel walls do not suffer the intense irritation, and thrombosis does not take place rapidly enough; the successive bacilli find an opportunity to invade the delicate young vessel wall itself and make their way through it.

In regard to the greater permeability of the lymph-channels and the more delicate structure of the coats, etc., which possess the same characteristics as blood-vessel walls, see pages 332, 333.

In the adult, in whom the lymph-channels and lymph-glands are narrower and less permeable, in whom circulation and metabolism proceed more slowly, the proteins become more concentrated. They advance more slowly and in a more concentrated form toward the periphery of the blood-vessel wall, which is thickened by the irritation; thrombosis and obliteration take place and block the way for the bacilli that follow after.

The older an individual the greater the tendency to protein retention, which may attain so high a degree as to produce complete encapsulation and bring on recovery. Nevertheless, however, even in the adult a few bacilli may accidentally enter the blood path before thrombosis has taken place and thus produce the scattered solitary tubercles in various organs which are often found in phthisical patients.

The complete embedding of a vessel in a mass of caseous material, such as occurs in phthisis which spreads by aspiration, causes an irritation of the walls by proteins in the entire periphery and leads to thrombosis much more readily than when the outside of a vessel only comes in contact with a tuberculous focus; hence it is much less likely to lead to miliary tuberculosis than the latter condition.

Miliary tuberculosis would be even more common in children were it not that the focus is usually situated within the glands, where a certain reduction of the poison takes place.

It is also possible that in phthisical subjects, owing to the continued ingestion of tubercle proteins containing substances that hasten coagulation, the blood clots more readily; it is also possible that the vessel walls are in a more irritative condition on account of the proteins.

But, after all, it is not at all uncommon to find in phthisical cadavers on careful microscopic examination if not a general miliary tuberculosis in the anatomical sense, that is, miliary or submiliary nodules, at least the beginning of tuberculous nodules in widely separated organs; or isolated bacilli that have not yet produced any reactive phenomena in the surrounding tissue; or even during life, but especially toward the end of life, tubercle bacilli in the blood. The significance of this phenomenon, which in a way represents the first clinical stage of miliary tuberculosis, was pointed out on page 633.

PREDISPOSING FACTORS.

While miliary tuberculosis may occur at any age, youth appears to favor its production. As regards sex, we have no definite knowledge of its influence.

Tuberculosis in general is much less widespread among children than among adults, and one would therefore suppose that miliary tuberculosis would also be more infrequent; but when a tuberculous focus is once present in the body, there are several reasons why a general infection takes place more easily and comparatively more often in the child than in the adult.

Mechanical or other irritants, inflammation and the like, affecting a tuberculous focus and its surroundings, may assist in the production of a miliary tuberculosis by loosening the bacilli that have become wedged fast in the caseous material and favoring either a direct rupture or a gradual advance of the bacilli toward the blood-vessels, with or without a change in the blood-vessel wall. In this way the swelling and maceration of glands, which in children accompanies measles, whooping-cough, and the like, may in association with a latent glandular tuberculosis produce not only a dissemination of the germs in the immediate neighborhood, as, for example, in the lungs, but also rupture into a blood-vessel and lead to acute miliary tuberculosis. It is also possible that an exceptionally violent paroxysmal cough may rupture the capsule, just as pulmonary hemorrhage has been traced to the same accident.

During the tuberculin period, cases of miliary tuberculosis produced by tuberculin injections were also reported. In connection with what has just been said, the possibility of such an occurrence cannot be denied, although I myself among 420 cases treated with tuberculin did not meet a single case of this kind.

Traumatism is also a favoring factor for the occurrence of rupture, either directly by causing the fibrous capsule surrounding a tuberculous focus to burst, or indirectly by inflammatory reaction.

As both acute infectious diseases and traumatism are unquestionably much more common in children, the greater frequency of miliary tuberculosis in childhood is quite explicable.

Pregnancy and the puerperium (Schellong, Fischel, Chiara, and others) also appear to favor miliary tuberculosis.

Although operation upon a perfectly healthy part of an individual who is suffering even with advanced tuberculosis of the lungs is not followed by general tuberculosis, such an accident has frequently been observed after operations on tuberculous bones and joints, evidently because the blood-channels are open and readily take up the bacilli, or because the bacilli grow into the blood-channels (König and others).

According to the analysis made by Warthmann, out of 837 resections 225 ended fatally from acute miliary tuberculosis, "the onset of which could at least with great probability be traced to the operation." But a more careful scrutiny of these cases shows that many of the cases of miliary tuberculosis included in the number cannot be attributed to the operation.

Similar observations are said to have been made after operations on rectal fistulæ.

In most of these cases it is probable that only a few bacilli entered the blood-channels and deposited themselves in some organs or blood-vessel, from which the general infection took place secondarily, and that the bacilli did not enter the blood in large numbers. This view is supported by the finding of blood-vessel tubercles in bone tuberculosis, as Benda frequently had occasion to show.

How large a part chance may play in this form of miliary tuberculosis following operative interference is shown by a case of Demme's. A child suffering from lupus was to be operated upon the next day. During the night severe venous hemorrhage occurred in a venous node, and two days later the child fell into a stupor, the temperature reached 41.8° C. (106° F.) and the pulse 148. On the fourth day there was another hemorrhage, followed by collapse and death. The autopsy showed an extensive miliary tuberculosis, which, if it had occurred a short time after the operation, would undoubtedly have been attributed to the surgical intervention.

Miliary tuberculosis has also been observed after the rapid disappearance of tuberculo-scrofulous glands, after pleurisy, peritonitis, etc., especially after the rapid absorption of pleuritic exudates; in the latter case, perhaps owing to the fluid being taken up rapidly by the blood-vessels, the plugs of bacilli and clots contained in the fluid are washed away and carried into the general circulation.

As in the case of many other infectious diseases, so in miliary tuberculosis worry and grief and similar causes have always been cited as etiological factors. There is no doubt that worry and grief, which are only too faithful in their attendance upon many human beings throughout life, do not spare those who fall a prey to miliary tuberculosis. No definite connection with any one of these factors has ever been established; but they cannot be entirely excluded, because they often go hand in hand with insufficient nutrition. That emaciation and loss of body-juices predispose the individual to miliary tuberculosis, as Jürgensen, Eichhorst, and others point out, is, I believe, explicable by the fact that in the ill-nourished individual the absorption of protein goes on more rapidly and the dissemination of the bacilli is thereby facilitated (see page 441).

Many authors mention the influence of climate and the weather on the production of miliary tuberculosis. Lebert in Zürich observed that the cases were somewhat more numerous in April and May; Buhl made a similar observation in Munich, and Virchow found that the disease was most common during the first months of summer. Litten, Eichhorst, and Benda unanimously report the same experience. Virchow and Abelin even go so far as to speak of the epidemic occurrence of the disease.

Aside from chance, which must play an important part when such small numbers are under consideration, the only explanation for the massing of cases at certain times of the year is that measles, whooping-cough, diphtheria, as well as simple catarrhs occur with great frequency or even epidemically at certain seasons of the year, and it is obvious that the sequelæ of these diseases, among which miliary tuberculosis figures very largely when certain conditions (latent glands) are fulfilled, are also more common at such times. In this way it is possible that miliary tuberculosis might in itself simulate an epidemic.

It has also been asserted that the development of miliary tuberculosis is favored by an antecedent attack of typhoid fever, and Cless, Burkart, and others have reported cases in which the two diseases were combined. But the combination is by no means frequent, although of some importance as refuting the view formerly advanced (by Rokitansky) that typhoid fever and miliary tuberculosis exclude each other mutually.

CHAPTER II.

PATHOLOGY.

In general miliary tuberculosis the ability of the tubercle bacilli to form nodules is most clearly seen. The nodules are characterized by the presence of tubercle bacilli, which are most abundant and thickest in the younger nodules, diminish in number as caseation begins at the center, and in the large nodules, the seat of advanced caseous degeneration are often seen only at the periphery and in scanty numbers.

The pathological findings vary greatly according as one or several successive invasions have taken place and according as many or only a few bacilli have entered the blood; again, according as living bacilli derived from a young focus or dead germs have been chiefly active, and according as tubercle bacilli alone or other bacteria, derived from a focus in which there is mixed infection, are present.

When miliary tuberculosis is the result of a single irruption, the nodules are all at the same stage of development; when several irruptions have taken place, on the other hand, their ages are different. For example, in an organ or in a pulmonary lobe there may be tubercles the size of a millet-seed, in others they may be as large as the head of a pin, in a third even larger—either commingled or in separate groups, depending on whether the infection has taken place from the same or from another focus. When only a few bacilli enter the blood-stream, the nodules produced are few in number and may attain a very large size before causing the death of the individual. When large conglomerate tubercles, such as may be present for some time without producing any marked disturbances not only in a less important organ but even in the brain, are found in acute miliary tuberculosis, they are to be ascribed to an old infection.

When living bacilli chiefly are taken up by the blood, the proliferative processes and tubercle formation are more marked; while, on the other hand, when dead bacilli are taken up, the toxic phenomena predominate.

After a copious invasion by tubercle bacilli, which, since it is the cause of general miliary tuberculosis, interests us chiefly in this connection, the tubercles are distributed over most, if not all, the organs of the body with a fair degree of uniformity; with the reservation, however, that in the individual organs the size of the afferent vessels, the quantity of blood contained in the parenchyma and the size of the capillary network influence the deposition of the bacilli. The massing of unusual numbers in a particular organ is usually explained by special structural and pathologic conditions obtaining in a particular case, and it is not necessary to assume a special predisposition of the organ in question.

Depending on the length of the interval between irruption and death, the tubercles appear as barely visible whitish dots the size of a grain of sand, or as gray, transparent miliary nodules. If the interval is still longer, the tubercles have a yellowish center, or the entire growth is cheesy.

THE VARIOUS ORGANS.

The **lungs** in miliary tuberculosis usually contain a more abundant crop of tubercles than the remaining organs, because after the rupture of a systemic vein or the thoracic duct these organs form the first filter through which the tubercle bacilli have to pass, and also participate by virtue of their nutrient vessels in any rupture into the pulmonary veins or into the aorta. Both lungs are, as a rule, uniformly infiltrated with numerous nodules, which frequently exhibit an inflammatory reaction at the periphery. The nodules feel hard; the surface of the lung on section appears dark red and finely granular. The lung contains a little less air than normal, is blood-red, and sometimes edematous and distended. A sanguineous fluid usually follows the knife as the cut surface is scraped and oozes from the bronchi, which are usually catarrhal and reddened. On careful examination the tubercles are frequently found on the intima, especially of the veins, as Orth and Mügge first demonstrated.

Within the **spleen** numerous miliary nodules and others even smaller are also found. They are surrounded by a red areola and closely resemble the follicles, from which they are distinguished by closer aggregation, greater prominence and more distinct delimitation. They are also firmer and harder than the follicles and are readily picked out with the point of a knife, while follicles tear when an attempt is made to pick them out in this way. The spleen may be considerably enlarged (according to Litten, in 70 per cent. of the cases), soft, and occasionally present fibrinous deposits.

The surface and the parenchyma of the **liver,** which often is very much enlarged, are almost without exception covered with minute tubercles, often so small as to be barely visible. The invasion of bacilli may take place through the portal vein or through the arterial blood, according as the primary foci occupy the intestine or some other part of the body. The nodules are found in the inter-acinous connective tissue and in part also in the interior of the hepatic lobules; they are often confluent and frequently produce interstitial inflammation. According to Arnold, they also produce proliferation of the bile-ducts. Heller and especially Simmonds emphasize the frequency of bile-duct cysts, especially in children dead of acute miliary tuberculosis.

In the **kidney** the tubercles develop chiefly in the cortical substance. On the surface they appear as grayish-white patches and later as slightly prominent nodules, sometimes surrounded by peripheral inflammation and often resembling small abscesses. They frequently follow the course of the *arteriolæ ascendentes*, and are arranged in rows like a necklace of beads. When the course is more chronic, the eruption of tubercles sometimes takes place in the distribution of one of the branches of the renal artery.

In the **bone-marrow** tubercles appear in almost every case; but, owing to the exceedingly short duration of life, they do not attain to any size. In the joints nodules are also found at times without any changes in the synovial membrane.

The **serous membranes,** especially the pleura, peritoneum, and pericardium, being comparatively poorly supplied with blood-vessels, are not affected to the same extent in a purely hematogenous tuberculous infection as the more vascular glandular organs. When they are involved, they appear often as if strewn with sand or covered with fibrinous deposits. Disseminated tubercles in the pleura are often surrounded by a hyperemic areola. On the parietal and visceral layers of the peritoneum, and especially in the omentum, numerous white, firm miliary tubercles frequently make their appearance. When the nodules are isolated, the phenomena of inflammatory reaction are usually absent. Endocardial and subendocardial tubercles are found almost constantly, and according to Weigert's assertion chiefly in the region of the *conus arteriosus* as far as the large papillary muscle; next in frequency, on the endocardium of both ventricles, especially at the septum.

Miliary tubercles are also found in the **meninges,** particularly in the pia mater, and sometimes also in the brain-substance. This is the case chiefly in children, and is usually associated with the presence of a milky, turbid, often gelatinous, serous or fibropurulent exudate at the base of the brain. Disseminated tubercles may also make their appearance in the spinal cord and its membranes.

The frequent occurrence of tubercles in the choroid—according to Cohnheim in all, according to Litten in 75 per cent. of cases of general miliary tuberculosis—is due to the vascular character of the membrane.

The **thyroid gland,** as Cohnheim has shown, frequently, and according to Weigert and Chiari almost regularly, takes a part in the tubercle formation. In addition, the rare occurrence of miliary tubercles on **mucous membranes,** in the larynx, pharynx, nose, and intestine, may also be mentioned.

In children suffering from a severe degree of general chronic tuberculosis Kaufmann observed hematogenous tubercles in the **stomach.** Occasionally, when the gastric mucous membrane is covered with tenacious mucus and intensely injected and presents no ulcers or losses of substance visible to the naked eye, microscopic examination not infrequently reveals miliary tubercles deeply embedded in the mucosa (Wilms, Simmonds).

Hanau on several occasions found large recent gastric and duodenal ulcers, which had originated in hemorrhagic scabs and were explained by him as of embolic origin.

The testicles, epididymis, prostate, suprarenal capsules, urinary bladder, pancreas, and more rarely the placenta (Lehmann, Schmorl-Kockel) show by the presence of disseminated eruptions of tubercles their tendency to take part in the process. In the ovary the tubercles appear to be exceedingly rare. Small flat tubercles are sometimes found in the uterus, and occasionally also in the tubes, the mucous membrane of which is in such cases frequently reddened. Miliary tubercles in the vulva and vagina were observed by Davidsohn.

Hematogenous muscle tubercles, circumscribed in certain areas, are exceedingly rare both in ordinary cases of tuberculosis and in the miliary variety (cases of Schuchardt, Weigert).

Many of the smaller organs escape the scrutiny of pathologists, and for that reason appear to be less frequently involved.

Finally, mention should be made of tuberculous infarcts, especially in the kidney, spleen, and lung (Nasse, Huguenin, Klebs, Hanau, Sigg), and punctiform hemorrhages in many organs, suprarenal capsules, brain.

In the **skin,** in which the tubercle bacilli after they effect an entrance can develop only very slowly, if at all, on account of the low temperature, tubercles are exceedingly rare and apparently develop only when the bacilli have entered along with other bacteria, which, so to speak, help them to become visible. Cases of this kind have been communicated by Heller, Peter, Meyer, Leichtenstern.

SOURCE.

On minute examination the source of a miliary tuberculosis is found in some region of the body in the form of an old focus, already referred to in the chapter on "Etiology," which has either been produced directly from the outside or is itself derived from a focus produced from the outside. The so-called irruption site of a miliary tuberculosis is found in a blood-vessel either lying within or closely contiguous to a focus, especially a vein. The frequent localization of this irruption site in pulmonary veins and in the thoracic duct has already been discussed at length in another place (page 639).

The special frequency of miliary tuberculosis in certain organs gives a clue to the probable position of the irruption site. For example, if tubercles are most prominent in the liver, the original focus must be sought in the distribution of the portal vein. If the tubercles in the spleen, liver, and kidney are most numerous, the search must be made chiefly in the pulmonary veins. When both lungs are chiefly and uniformly involved, the starting-point of the disease will probably be found either in the thoracic duct or in one of the systemic veins.

At the original focus we find either that the bacilli have invaded the vessel wall in enormous numbers or, what is much more frequent, a true blood-vessel tubercle is discovered—a grayish-yellow or reddish-white, club-shaped formation, attached to the submucous tissues and not quite filling the lumen of a blood-vessel, resembling a so-called fibrin coagulum. The surface is smooth and reflects the light, or may be slightly rough; the surface toward the interior is somewhat opaque, indicating a former ulceration. The blood-vessel tubercle often has a drop-like or polypoid appendage, about 20 mm. or more in length, projecting into the lumen of the blood-vessel—a phenomenon explained by Weigert on the supposition that the tuberculous mass during its gradual encroachment on the lumen is deflected by the blood-current. In the thoracic duct the foci are found chiefly in the neighborhood of the valves. Benda once found an aorta tubercle on the floor of an atheromatous ulcer. Frequently a connection with an extravascular focus can be demonstrated; in some cases, however, only by means of serial sections.

Not infrequently several foci or numerous miliary tubercles can be found in the vessels, particularly in the thoracic duct.

When the blood is flooded with an abundance of infectious germs, death occurs so early on account of the extensive absorption of protein that the further development of the individual tubercles is arrested.

In addition to the changes just described which correspond to the picture of pure acute general miliary tuberculosis, there are other cases in which the irruption of the entire mass of bacilli is preceded by the entrance of small numbers, perhaps only isolated germs, into the circulation as a kind of prodromal phenomenon. The tubercles produced by the latter may attain a considerable size, as the organism suffers but little and the course is at first chronic. Accordingly the picture of a chronic tuberculosis is found as a concomitant of acute miliary tuberculosis.

The changes in the lungs have been discussed at length in the section devoted to "Pulmonary Tuberculosis."

Within the spleen nodules of the most various sizes are found, with a cheesy and softened center and surrounded at the periphery by young nodules.

In the liver large cheesy conglomerate tubercles are rare. Orth, for example, described a tuberculous node as large as a fist. In the bile-ducts the nodules range in size from that of a pea to that of a hazel-nut and contain bile-stained, softened, cheesy masses; or correspondingly small cavities may be formed.

In the kidneys the disease, unless life is extinguished earlier, leads to extensive caseation of the pelvis of the kidney and of the calices, and then to tuberculous renal phthisis and a melting-down of the entire tissue of the viscus and its conversion into a sack filled with pus and the products of cheesy degeneration.

The epididymis, more rarely the testicle, may become enlarged and may contain one or more caseous nodules, the parenchyma being more or less completely destroyed. The tunica vaginalis is involved in the process, becomes the seat of exudative inflammation followed by thickening, adhesions are formed, and rupture finally takes place toward the exterior with the formation of a fistula and the protrusion of a fungoid mass.

In the thyroid gland it is rare to see large tuberculous nodules.

In bones extensive granulation tissue, tuberculous infiltrates, and the changeable picture of caries are produced. Tuberculous granulations may infiltrate the periosteum and adjoining soft parts, undergo cheesy degeneration and softening, and form a cold abscess.

In the serous membranes, peritoneum, pleura, and pericardium, when bacilli have entered the serous sac as a result of rupture of individual hematogenous tubercles situated on the membrane, or in some other way, the tubercles are rapidly disseminated because the two layers of the membrane are in constant movement. Owing also to the absorptive power of the tissue, the tuberculous proteins are taken up in large quantities and inflammatory products, serofibrinous, and frequently also hemorrhagic exudates are produced. When pyogenic bacteria effect an entrance at the same time, purulent exudates, and later in the course of the disease numerous adhesions, or more or less extensive obliteration of the cavity take place.

Special changes are often produced in the omentum, which becomes converted into a mass of board-like hardness, thicker than the finger.

When a few bacilli have been carried to the brain and life is prolonged for some time, the individual tubercles collect to form conglomerations as large as a walnut or even as large as a hen's egg or larger, with a cheesy center and a periphery consisting of grayish-red granulation tissue and later of fibrillar connective tissue.

Depending upon the position of the primary focus, the pathologic findings present material variations when, in addition to hematogenous infection and sometimes preceding it, a dissemination of the tubercle bacilli has taken place through the lymphatics.

Marked involvement of the immediate neighborhood of the primary focus and extensive nodule formation in the serous cavities point more to a lymphogenic than to a hematogenous origin.

MIXED INFECTION.

Although in a general way acute miliary tuberculosis has been designated the purest form of tuberculosis, the statement is to be accepted only with certain reservations; for even the miliary tubercle is not always the product of the tubercle bacillus alone. Apparently it may also owe its existence to the combined action of the tubercle bacillus and some other pathogenic bacterium. In two cases of acute general miliary tuberculosis that developed after pulmonary phthisis of some standing I was the first to find in the sputum (secretion from a cavity), after washing it, once the pyocyaneus and another time the pyogenes aureus in extraordinary quantities and almost in pure culture. In both instances I succeeded in demonstrating post mortem within the disseminated miliary tubercles of the liver, spleen, and kidney the pyocyaneus and pyogenes respectively, in addition to tubercle bacilli. An absolute proof of the fact that these mixed bacteria were derived from the same focus as the tubercle bacilli and were intimately mixed with the latter before they entered the circulation is furnished by the finding of these associated bacteria in the miliary tubercles themselves and nowhere else.

Besides Koch, who observed micrococci in association with tubercle bacilli in the capillaries of the lungs and spleen in acute miliary tuberculosis, Babes, Kossel, and Sata also saw mixed infections in acute miliary tuberculosis. Heller's case of miliary tuberculosis of the skin in a certain sense also belongs to this category.

CHAPTER III.

SYMPTOMS.

Acute general miliary tuberculosis presents a variety of disturbances and changes, for the proper understanding of which it is necessary to keep in mind the pathogenesis of the disease. They are explained in part by the toxic action of the tubercle proteins and in part by the local formation of tubercles. The toxic effect manifests itself earliest and is most intense. From the moment when rupture takes place and produces a miliary tuberculosis, all the proteins collected in a cheesy focus and the decomposing bodies of the dead bacilli are taken up by the blood, the toxic effect manifesting itself not at once but, just as after tuberculin injections, only after four to twelve to twenty-four hours in the usual familiar way. Sometimes the soluble poison may make its way through the denuded wall of the vessel some time before the occurrence of rupture, especially in the veins, where the negative pressure causes a sucking action. In such a case a prodromal stage, during which the phenomena are but slightly marked, ushers in the acute disease.

The poison that is taken up at the irruption site differs both qualitatively and quantitatively, according to the nature of the ruptured focus. Qualitatively there is a difference as regards the age of the tuberculous focus. The poison contained in a small, young focus is not only less in quantity, but apparently also contains an excess of the less noxious metabolic products; whereas in old cheesy foci containing great numbers of dead and decaying bacilli the proteins are in excess.

The quantity of poison taken up is also extremely variable. It depends on the size and age of the focus and, to a certain extent, on the size of the irruption site (the ulcer) and probably its seat as well, inasmuch as the negative pressure in the venous channels facilitates absorption. The quantity varies also according as the starting-point remains open for some time or is at once closed by fibrin derived from the passing blood either permanently or only temporarily, in which case rupture takes place anew. This process may repeat itself several times in the form of so-called relapses, as the different layers in the blood-vessel tubercle abundantly prove. It is also to be remembered that several tuberculous blood-vessel foci formed approximately at the same time are often present in the body and rupture either synchronously or in alternation one with the other.

The quantity also and, if I may say so, the quality of the bacilli injected into the blood-channels vary according to the nature of the original focus. The small number of bacilli that are sparingly cast off by a small tuberculous focus are not sufficient to produce an acute general miliary tuberculosis, while a larger focus will send out whole masses of pure cultures into the circulation. One of these bacillary masses, after being carried away by the blood, becomes finely divided by the friction of the blood-corpuscles against each other, and a number of the bacilli are also taken up by the white lymph-corpuscles. These conglomerations and flocculi possess a considerable degree of consistency and coherence, as may be seen in the cultures and in cadavers,* and division therefore does not always proceed very rapidly. But even if a few bacilli separate from the general mass, the latter nevertheless occasionally enters as a whole into a small artery supplying only a single organ. As the vessel continues to divide and the lumen becomes smaller and smaller, the mass is eventually arrested at the point of division as on a saddle and temporarily obstructs the blood-stream, but ultimately is broken up into its constituent parts, the bacilli. The entire process resembles embolism, except that an embolus is still more coherent and occludes the vessel while the cheesy mass breaks up. This coherence explains why only one organ is frequently attacked by miliary tuberculosis, even when rupture has taken place into the greater circulation; and this selection of a special organ cannot be used as an argument in favor of a "peculiar predisposition," as it is due to accident or to the laws governing the circulation of the blood and to the division of arteries, which may take place at a more or less acute angle.

As regards their quality, also, bacilli are not indifferent. When a tuberculous focus is comparatively recent, most of the tubercle bacilli that are carried off are still in the full vigor of life, and during their subsequent development the formation of tubercles is the most prominent feature. In the cheesy focus of some standing, which has been relighted by some accidental event such as saturation with some morbid inflammatory product or a traumatism, dead bacilli predominate among those that are carried into the circulation. These dead bacilli do not lead to independent tubercle-formation, since, as the animal experiments of Maffucci first showed, the most they are able to effect is a rudimentary formation of nodules; but as they break down they may damage the entire organism considerably as a poison.

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* I need only remind the reader of the small hard masses consisting almost entirely of bacilli which are found in the sputum.

These differences in the conditions, the predominance of one factor or another, enable us to understand that a general miliary tuberculosis does not, like many other infections, as typhoid fever, for example, run a typical course. It also explains the frequent changes and apparent irregularities in the phenomena. As the tubercle develops it exerts a mechanical effect upon the periphery, the parenchyma, the vessels, and the nerves, and through the agency of the diffusible poisons also a chemical effect not only on its immediate neighborhood but also upon the entire body; for while only a very small amount of transudate is produced by a single tubercle, yet the entire mass, consisting of 1000 or 100,000 individuals, produces a respectable quantity of tuberculin in the course of a day. Again, the conditions for absorption are as favorable as could be imagined; for absorption depends much less upon the total mass of the tuberculous foci than it does upon the surface presented to the tissue endowed with the power of absorbing. A large tubercle has a smaller surface area than a number of small ones, which taken together are equal to it in volume. Assuming in the case of a phthisical patient that a cheesy focus is 5 cm. in diameter, its contents would be equivalent to the contents (volume) of 125,000 miliary tubercles of 1 mm. diameter. But the surface in the case of a large focus is equivalent to 7500 sq. mm., while the surface of the miliary tubercles is 375,000 sq. mm., or fifty times as great. In addition, the cheesy focus is often encapsulated, while a recent tubercle is everywhere surrounded by tissue capable of absorbing. This is proved by its rapid growth; for, if it were encapsulated, it would soon be smothered, so to speak, in its own poisons. I do not, therefore, share Benda's view, which explains the clinical symptoms in part by the freshly disseminated tubercles.

As the toxic effect is the most prominent feature in acute general tuberculosis, the general symptoms are correspondingly the most prominent in the clinical picture, while local symptoms often do not manifest themselves until late in the course of the disease. The general symptoms are observed at a time when it is impossible to speak of miliary tuberculosis in a pathologic sense, and when, if death occurs from a sudden accident, neither miliary nor submiliary nodules are found in the cadaver, which at most reveals bacilli scattered through the organs. The clinical conception of miliary tuberculosis is therefore more comprehensive than the pathologic.

FEVER.

The most constant of the general symptoms is a considerable degree of fever. The sudden irruption of bacilli and poison (toxins) into the blood is marked by a rise in temperature, often not preceded by any prodromal symptoms. The onset of fever may be ushered in by one or two chills, after which the temperature rises rapidly, not infrequently on the first or second day to the maximum height of 39.5° to 40° C. (103° to 104° F.) and over that is reached during the entire disease. As a rule, the temperature does not rise so high as in typhoid fever. The fever has no definite type, altering its character in accordance with changes in the causative factors. Irregularity is its most important diagnostic feature and is most marked in subacute cases. The apparent absence of any regularity finds a definite reason in the changes that mark the process of absorption and in the relapses, etc., which have been outlined above.

Sometimes the pyrexia persists in the form of a continued fever, or it assumes an irregularly remittent character, or it may be intermittent for a short time or even for several days. Abrupt rises to 40° C. (104° F.) and over, with rapid fall to subnormal and collapse, make up the picture of hectic fever. Death occurs either in agonal hyperpyrexia or in collapse (34° or even 32° C.—93.2° or 89.6° F.).

Persistent high temperature, sometimes simulating that of typhoid fever, is found, especially in very acute cases with an abundant crop of tubercles and in the absence or partial absence of cerebral involvement; while abundant tubercle formation in the brain acts as a depressant to the temperature and quite frequently causes marked fluctuations in the fever curve. More frequently than in other febrile diseases we observe in acute miliary tuberculosis, in addition to the irregularity, an inverse type, *i. e.*, exacerbation of the fever during the morning hours with remission toward evening (Bruniche). The phenomenon, however, rarely lasts more than a few days.

While in the case of a healthy person the fever acts like an alarm-signal and clearly points out the onset of a grave disease, the transition to acute tuberculosis in the case of a phthisical patient, especially one who has had hectic fever, is often practically imperceptible because of the slight increase in the fever.

That considerable fever is a regular symptom of miliary tuberculosis is a rule that has many exceptions. Sometimes the temperature rises only to a moderate height, about 38.0° to 38.5° C. (100.4° to 101.3° F.), or it may remain quite normal, although the time of fatal termination is not thereby materially delayed. Cases of this kind have frequently been observed. In one case of a girl, for example, who died after three weeks, the temperature never exceeded 38.5° C. (101.3° F.); the autopsy revealed widespread general miliary tuberculosis (Litten).*

In another case the temperature at first was 38.7° C. (99.8° F.), which was the highest point reached, and five days later became normal.†

The depressant influence of meningitis has already been referred to. Among 52 cases of acute miliary tuberculosis in the Freiburg clinic 9 of this type were found in which the temperature reached 58° C. (100.4° F.) only at exceptional times, and three of these were cases of very severe general tuberculosis (Reinhold). Without meningitis an afebrile course sometimes occurs, especially in old persons. In such cases miliary tuberculosis presents itself solely in the guise of a diffuse bronchitis or degeneration of the heart. An example of this character is a case cited on page 671 from Hager of ambulant miliary tuberculosis, if such a term may be used. Leichtenstern observed an afebrile course in a child with cirrhosis of the liver, in a patient with chronic nephritis, and in two children with extreme general atrophy. The purest cases of a completely afebrile course are those of Joseph in Fürbringer's clinic.

A man twenty-eight years old, who for two years had suffered from cough which was gradually getting worse and from expectoration, applied for admission to the hospital in a state of extreme lassitude and dyspnea. Although there were no cerebral phenomena, the temperature ranged from 36.0° to 37.2° C. (96.8° to 98.9° F.) during the six days that the patient was under observation. The autopsy showed an abundance of gray, cheesy miliary nodules in the lung and liver and a few scattered nodules in the spleen, but no changes in the brain or meninges. Two other cases were quite similar to this one.

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* In this case the disease began with violent hemoptysis; in another the temperature fell after profuse epistaxis from 38.5° to 37.2° C.—101.3° to 98.9° F.—(two days later death occurred with a temperature of 32° C.—89.6° F.). Litten is inclined to hold the hemorrhages, vomiting, and diarrhea responsible for the drop in the temperature.

† Annalen des Münchener Krankenhauses.

Eichhorst and Lange also report cases of this kind.

The afebrile course may be explained on the theory that in many individuals the heat-center is, so to speak, in an immovable condition and is insensitive to certain bacterial poisons. A parallelism is found in the afebrile course of typhoid and pneumonia, in the so-called ambulatory cases. These remarks remind me of a patient whom I treated during the period of tuberculin. In spite of great destruction of lung tissue he was said never to have had any fever. He received as much as 1 gram of pure tuberculin, to which he reacted by some feeling of lassitude, but never by the slightest rise of temperature. About six weeks later he died, as was to be feared from the condition of the lungs.

It is not to be forgotten, however, that increase in temperature is only one of the constituent parts of fever. Although, therefore, the heat-center may be insensitive to the bacterial poison, it does not prove that the entire body is equally insensitive; the truth of this is shown by the extreme prostration that is observed in these afebrile cases of miliary tuberculosis and by the fact that death is not delayed.

A contrast to this indifference of certain nerve-centers is found in those rare cases of phthisis in which the patients for weeks and months have high fever of 39° C. (102.2° F.) and over (see page 602), and go about without suffering any considerable loss of strength; in such individuals the poison evidently affects the heat-regulating apparatus and has but little influence on the other nerve-centers.

VASCULAR SYSTEM.

The pulse, as a rule, is very frequent, often from the beginning 120 to 150; that is to say, it is more frequent than would be expected from the temperature. It is rarely full. On the contrary, it is usually small and sometimes barely palpable. As a rule, it is soft, and occasionally, but more rarely than in typhoid fever, dicrotic. The lowering of blood-pressure, which is the effect of the tuberculous toxins, has already been referred to. (See pp. 392 and 393.)

In rare cases and practically only in older persons the pulse may be less than 100 beats in a minute. Another cause of slow pulse is the complicating meningitis.

The contractions of the heart are accordingly very much accelerated and weak. As the strength of the heart diminishes, congestion develops in the venous system and in the lungs, and often leads to fatal edema. For physical signs see page 664.

In rare cases a hemorrhagic diathesis develops, and hemorrhages from the nose, the gums, the intestine, the retina, etc., take place (mixed infection?).

RESPIRATORY ORGANS.

Very early in the disease symptoms manifest themselves in the respiratory tract. The first sign is often a severe, distressing cough, caused not so much by the general toxemia as by the presence of innumerable tubercles in the lung, which irritate the nerves of the vagus fibers. The paroxysms of coughing are sometimes so severe that the contraction of the thoracic abdominal muscles and attendant irritation of the pleura may cause excruciating pain without bringing much expectoration to the surface. During the subsequent course, especially as the cerebral symptoms increase, the cough subsides.

Marked acceleration of breathing is practically the rule. It frequently precedes the rise in the pulse-rate and may attain 40, 60, and in children 90 respirations in a minute. With it there develops very soon a severe dyspnea, which curiously is not sufficiently explained by the physical signs and appears to be caused by the irritation of the terminations of the vagus fibers in the lungs by the tubercles (Ruehle), or possibly by the presence of tubercles on the diaphragm, a not infrequent observation (Reinhold). The dyspnea sometimes goes on to the production of asthmatic attacks and orthopnea of the most exaggerated type, forcing the patient to sit up straight in bed. Exceptionally the dyspnea may develop during the last days of the disease, and then becomes rapidly worse. In many cases distinct Cheyne-Stokes breathing is observed.

Sometimes acute emphysema develops in the course of acute miliary tuberculosis. This phenomenon, which has been especially pointed out by Burkart and Litten, is probably to be explained by the violence of the cough.

Aside from complications, the expectoration is of course scanty, frothy, air-containing, and mucoid, resembling the sputum observed during the stage of reaction in non-phthisical tuberculous patients treated with tuberculin. Sometimes a few streaks of blood due to capillary ruptures, are observed, and in very rare cases the expectoration is rusty even when there is no complicating pneumonia. These slight hemorrhages find a parallel in other organs where the tubercle-formation leads to small ecchymoses; for example, in the brain, stomach, and even in the skin. Large hemorrhages are observed only when phthisis is also present.

Later in the course of the disease, especially during the subacute stage, the expectoration may become more abundant, mixed with formed elements, yellowish, and free from air.

A bronchiolitis, often involving the minutest air-passages, is often observed early in the disease. When old foci are already present in the lung, the symptoms that they produce combine with the new set of symptoms and in some cases undergo only an indistinct exacerbation.

NERVOUS SYSTEM.

Many of the more important symptoms are derived from the central nervous system. When the meninges are the seat of tubercle-formation and of other complicating processes, the nervous phenomena predominate to such an extent in the clinical picture that the remaining disturbances—in the lungs, for example—are forced into the background and completely obscured; but even without special involvement of the meninges of the brain marked disturbances that cannot be attributed to the fever as such, but seem to depend partly on the fever and partly on a simple toxemia, are quite frequently observed. Analogous phenomena are sometimes noticed after tuberculin injections.

With the sudden onset of the disease, or in some cases during the preliminary toxin-absorption a little while before the onset, dull headache, sometimes in the frontal region and vertex, a certain degree of hebetude, tinnitus aurium, somnolence, and vertigo make their appearance. Sleep becomes restless, and terrifying dreams distress the patient so that he is apt to cry out during his sleep. Later he falls into a half-waking, delirious condition; when spoken to, he looks around him in astonishment for a moment, but rapidly regains consciousness and answers intelligently, only to relapse into his semicomatose condition. Later he becomes apathetic, the sensory sphere is more and more clouded, and a stuporous condition develops, often interrupted by coma or furious delirium; at last death takes place in coma.

Sometimes the disturbances of consciousness do not develop so gradually, but come on abruptly, without warning, like an apoplectic attack, and last until the end.

In very rare cases the patient retains full consciousness until the last hours and exhibits only profound prostration and despondency. The expression of the face, especially when there is dyspnea, is often anxious and the patient looks as if he were imploring help.

Sometimes the miliary tuberculosis is attended by severe, rapidly increasing muscular weakness, rapid loss of strength, and a feeling of extreme lassitude and exhaustion, which often manifests itself in muscular tremors. This is not due to the fever alone, but must be ascribed in part to the specific action of the tubercle proteins, as it sometimes develops rapidly even when the fever is inconsiderable. Sometimes hyperesthesia, convulsions, gnashing of teeth, sighing, and sudden crying out are observed.

In meningeal tuberculosis the nervous symptoms are exaggerated. There may be frequent vomiting, irregularity of the pulse, strabismus, contraction and dilatation of the pupils, painful contraction of the neck muscles (exceptionally present without meningitis), stiffness of the neck, flexion contracture of the knee (Kernig's sign), paralysis in the distribution of the cranial nerves, convulsions, clonic spasm in the lower extremities, persistent sobbing and the like. For a more detailed description of the symptoms of tuberculous meningitis the reader is referred to the special article upon this subject.

DIGESTIVE ORGANS AND URINARY APPARATUS.

Even when the consciousness is not affected, the appetite is as a rule destroyed from the very beginning. The oral cavity and tongue are usually dry and covered with dark brown crusts due to small hemorrhages. In severe cases scorbutic ulcers are occasionally seen on the gums. Nausea and violent vomiting are most marked when the tubercles are localized in the meninges. The bowels are usually constipated; more rarely the patient has diarrhea, somewhat resembling that of typhoid fever, and exceptionally blood is found in the stools even when no tuberculous ulcers had been present before (G. Sée, Reinhold). The abdomen is normal, although it occasionally presents slight meteorism, sensitiveness to pressure, and often gurgling in the ileocecal region.

The loss of strength is often accompanied by striking emaciation, at times resulting in the loss of one-fourth of the body-weight (Wunderlich).

Corresponding to the profuse sweating that occurs, the quantity of urine is usually small; the secretion is dark and contains an abundance of urates and often small quantities of albumin; peptonuria is sometimes present. In children suffering from miliary tuberculosis of the kidneys anuria is occasionally observed (Rosenstein). When consciousness is disturbed, involuntary evacuation of urine and feces takes place.

SKIN.

According to the degree of dyspnea, the face, especially the nose and lips, and the nails often become cyanotic early in the disease. In other respects the skin is strikingly pale and rarely exhibits the redness peculiar to high fever or the circumscribed flush of florid phthisis.

Many patients suffer greatly from profuse sweats, with or without collapse temperature, resulting in the formation of sudamina and miliaria, especially on the trunk. Herpetic vesicles sometimes develop on the lips. Roseola, which was first observed by Waller and then by Jaccoud, Collin, Senator, Hager, Eichhorst, and others, is, on the whole, extremely rare, especially if the term "roseola" is not construed too liberally. Sometimes petechiæ or erythema nodosum may be seen (Reinhold). Miliary tubercles on the skin are rare exceptions. They have been observed by Heller, Pet. Meyer, and Leichtenstern, and are probably due, as in the case reported by Heller, to mixed infection.

In Leichtenstern's case, that of a boy four years of age, bright red, hard, conical papules, ranging in size from that of a poppy-seed to that of a hemp-seed at most, sharply outlined and rising on a perfectly normal base, appeared first on the face. Later similar papules made their appearance on the trunk and upper and lower extremities. There were never present at the same time more than twenty-eight lesions. Most of them, after persisting for from one to two weeks, gradually became paler and finally desquamated in fine scales and then disappeared; in others the apex of the papule was occupied by a minute vesicle or pustule, which rapidly dried up, after which desquamation occurred and the lesion disappeared. The process never went on to the formation of large papules, pustules, or small cutaneous ulcers. In the pus obtained from the pustules streptococci but no tubercle bacilli were found; in the papillary body innumerable tubercle bacilli were found embedded in the granulation tissue at the autopsy.

Toward the end of the disease edema often develops in the upper and lower extremities.

PHYSICAL SIGNS.

Owing to the development of tubercles in the lungs and the irritation caused by the proteins, the signs of diffuse catarrh are observed. Percussion as a rule reveals no changes aside from old foci or the remains of former morbid processes, such as a pleuritis and the like, because the miliary nodules are everywhere surrounded by air-containing parenchyma and are unable to modify the normal note. Occasionally in circumscribed atelectatic areas a somewhat empty, dull note is obtained, which may arouse the suspicion of pneumonic infiltration; but it is only temporary. As the tubercles increase and the tension of the lung tissue diminishes, the percussion note acquires a tympanitic quality.

On auscultation, exaggerated roughened vesicular breathing is heard, besides sibilant and sonorous râles and finely vesicular, or small crepitant or medium-sized or subcrepitant râles in the most various places, often over the entire extent of the lungs. The disproportion between these insignificant signs and the violent dyspnea are of diagnostic importance. Gradually, and only in exceptional cases quite suddenly, the signs increase and the pulmonary edema which ushers in the end develops.

Sometimes acute emphysema, probably caused by the violent cough, develops during the course of miliary tuberculosis, as Litten and Burkart especially have pointed out.

As a result of abundant tubercle-formation on the surface of the lung or of the pleura, where the two slip over one another, Jürgensen described an extensive fine soft friction murmur, heard at the site of its production and distinguished from ordinary pleural friction by the peculiar quality of the sound. It is not attended by pain and resembles a crepitant râle more than any other sound; but it is heard both during inspiration and during expiration. Jürgensen regards this friction murmur as pathognomonic.

Litten also observed a fine friction murmur somewhat increased by pressure. In one case, in which he heard this murmur at the apex of the heart, autopsy revealed the presence of groups of miliary tubercles in the initial portion of the aorta and opposite on the pericardium. In another case, in which the murmur was heard in the right hypochondrium, miliary tubercles were found on the surface of the liver and on the corresponding portion of the parietal peritoneum.

A similar but harsher friction sound was heard by Burkart, and at the autopsy was found to be due not to recent but to old calcified tubercles.

These phenomena are at best exceedingly rare. Ordinary friction murmurs, caused by pleuritic irritation with or without effusion, are much more common. The exudate when present is often hemorrhagic.

In the heart a systolic murmur is sometimes heard at the apex and the second pulmonic sound is sometimes accentuated. Dilatation and hypertrophy of the right ventricle are, as a rule, attributable to circulatory interference due to an old apical phthisis.

The spleen is usually painless and difficult to palpate on account of its softness. By percussion it is almost always possible to demonstrate enlargement of the organ, especially when there is no meteorism; the enlargement, as a rule, is gradual, and not so great as in severe cases of typhoid fever, nevertheless the organ occasionally swells to three or even six times its normal volume.

In very rare cases tubercles have been demonstrated in the larynx, on the vocal cords; such tubercles often break down very rapidly.

THE EYE.

A phenomenon that is especially important from a diagnostic standpoint is the appearance of tubercles in the choroid. They were first observed by Manz and Busch. Their existence during life was demonstrated by Gräfe and Leber, and their great diagnostic importance in miliary tuberculosis was first appreciated by Cohnheim. Among 52 cases of acute miliary tuberculosis reported by Litten they were found 39 times; among 87 cases of Demme, 19 times; and among 50 of Reinhold's, only 8 times.

Whenever they occur, they almost without exception attack both eyes. They appear as pale, grayish-white, later yellow, sometimes circular, sometimes irregularly oblong patches with somewhat indistinct edges; as they increase in size they cause a bulging of the choroid, which becomes particularly noticeable when the nodule is traversed by a retinal vessel; when the tubercle breaks down, the appearance of a depression (Litten) is sometimes presented. Sometimes the nodules are solitary; more often they appear in numbers of from 6 to 10. Cohnheim once counted as many as 52 nodules in the eye of a cadaver. They are irregularly scattered over the choroid and may be found in the optic papilla, in the macula lutea, or in the equatorial zone.

Other symptoms observed in the eye at different stages of the disease are, contraction or dilatation of the pupils, and in rare cases retinal hemorrhages, besides a number of other phenomena which need not be mentioned here as they belong to tuberculous meningitis.

CHAPTER IV.

COURSE, DURATION, AND TERMINATION.

COURSE.

Owing to the many possible combinations of symptoms, depending on differences in the causative conditions of miliary tuberculosis which are described in the beginning of the preceding chapter, and on the peculiarities both of the organ attacked and of the individual himself, the clinical picture and course of the disease are so extraordinarily variable that it is apparently very difficult to compare opposite extremes and show that they are due to the same cause. Certain unmistakable leading types, however, which were first described by Waller, are still recognized, and for practical purposes should be borne in mind.

THE TYPHOIDAL FORM.

The typhoidal form is so called on account of its similarity to typhoid fever, which is often so great that older physicians—for example, Engel—regarded "both dyscrasiæ as a single, albuminous dyscrasia." After a more or less distinct prodromal stage, marked by headache, malaise, loss of appetite and a feeling of weakness, fairly high, continuous, or slightly remittent fever of 39° to 40° C. (102.2° to 104° F.), with acceleration of the pulse and of the breathing and the rapid development of dyspnea and marked disturbances of consciousness, develops. Marked splenic enlargement, meteorism and roseolous rash, diarrhea, and intestinal hemorrhages may completely simulate the picture of typhoid fever. Death may occur within a short time amid the symptoms of profound prostration and before the condition of affairs has been cleared up by the development of any characteristic signs.

The foundation of such a course is a general severe intoxication of the body with the tubercle poisons without any marked local effect from the tubercles.

THE PULMONARY FORM.

The subjective and objective signs of lung disease predominate. An apparently healthy individual suddenly develops violent cough, at first dry and later with expectoration, lancinating pains in the chest, anxious expression of face, frequent pulse and extremely rapid respiration, to be followed after a few days by dyspnea and orthopnea, cyanosis, extreme weakness, and rapid loss of strength. The high fever with sudden onset ushered in by a chill, the physical signs of a severe catarrh, dulness,—transitory, it is true,—sometimes a tympanitic note in some areas, and the rust-colored sputum may give rise to a clinical picture which resembles either a croupous pneumonia or, especially in old persons, a severe febrile bronchitis with emphysema.

With rapid loss of strength, sometimes without disturbance of consciousness, death occurs from pulmonary edema.

This form is chiefly characterized by an abundant formation of tubercles in the lungs, which explains the most important clinical phenomena. The absorption of poison is not so great as to bring about death at once, and the individual tubercles have time to undergo a certain degree of development. Hence the local irritative effects are more pronounced and the course is less tumultuous.

THE MENINGEAL FORM.

When an abundant dissemination of bacilli takes place in the cerebrum, the irritative phenomena produced in that organ dominate the entire situation. The miliary tuberculosis in the lungs in such cases may be completely overlooked; sometimes it reveals itself by a few barely perceptible, peculiarly deep and accelerated respirations occurring in a condition of deepest coma (Strümpell). The patient complains of intolerable headache, which rapidly becomes worse; soon the consciousness becomes clouded, he becomes apathetic and rapidly sinks into a comatose condition, delirium develops and convulsive phenomena, stiffness of the neck, and disturbances of innervation of the ocular muscles appear. The temperature and pulse rarely attain so high a degree as in the preceding form and are rather characterized by their instability. The excessively frequent respirations and contractions of the heart characteristic of the pulmonary form are in part combined with the superficial breathing of meningitis, interrupted by sudden deep sighing inspirations and with intermissions and irregularities in the size of the pulse-waves (Ruehle). Death occurs in profound coma, sometimes after an agonal rise of temperature.

In children, especially small children, severe meningeal symptoms sometimes occur, trismus, epileptiform attacks, persistent convulsions, contractures, tonic muscular rigidity, and stiffness of the neck, which suggest a marked involvement of the cerebrum, although at the autopsy the meninges reveal no tubercles nor anything else except hyperemia and edema, as, for example, in some cases reported by Henoch.

The meninges are involved with especial frequency in childhood. Among 87 cases of acute miliary tuberculosis Demme found cerebral tubercles in all but 4.

Owing partly to the fact that absorption takes place more rapidly in children and young individuals, the general symptoms, or, in other words, the typhoidal form predominates in those periods of life; and, owing to the more frequent involvement of the brain, the meningeal form is also more common at that time; while in older persons the local symptoms and especially those of the lung predominate.

In addition to these principal forms and the various transitions from one to the other, there are a number of other clinical pictures: for example, those that run a fulminant course (Demme); or simulate delirium tremens (Waller); or forms in which the fever or often the entire symptom-complex exhibits a more intermittent character and reminds one of true intermittent fever.

Catti reports two cases observed in children which he characterizes as cases of the pharyngo-laryngeal type. The larynx and the adjoining portions of the pharynx, especially the soft portions of the tonsils and the base of the tongue, exhibited swelling, redness, and in one case ecchymoses, besides numerous gray, transparent, and in part miliary nodules, elevated above the surrounding level. The patients complained of dyspnea, and attacks of asphyxia occurred; the temperature was normal. Death occurred after three weeks with the signs of cardiac weakness and collapse. At the autopsy general miliary tuberculosis was found.

Frequently the severe symptoms are preceded by a prodromal stage marked by nervousness, lassitude, a feeling of weakness, slight febrile movements, or distressing almost dry irritative cough, dyspnea, and cyanosis. This stage may last one to two weeks and then the condition gradually or suddenly becomes worse.

The transition from an old chronic phthisis to miliary tuberculosis is often quite imperceptible; the ever-present phenomena of fever, dyspnea, and weakness become more marked, and headache and disturbances of consciousness are added; or the transition may be sudden and well marked, or delirium may develop. Sometimes in the meningeal form phenomena of spinal irritation. pain in the neck and girdle pains, stiffness, sensitiveness to pressure of the vertebral column and the neck are present (Reinhold). In this group of cases miliary tuberculosis often ends fatally in a few days or weeks, with ever-increasing weakness and without ever being recognized.

In old persons with weakness of the heart the onset is often unattended by any symptoms.

A steadily progressing course ending in death is the general rule in this disease. Not infrequently, however, temporary cessation and improvement take place. Aside from the deceptive fall in the temperature and the slowing of the pulse, which are due to an increase in the cerebral irritation and can only be regarded as masking the symptoms, there are cases in which the symptoms actually subside for a time. After a marked remission in the fever the temperature returns almost or quite to normal; pulse and respiration become regular again; consciousness becomes complete; and the patient even gains some strength. When we remember the differences existing in the pathogenesis of the disease, such periods of improvement are quite explicable. If a rupture has been followed by a pouring out of an abundance of proteins and comparatively few bacilli, the toxins may be excreted from the body in a few days, provided the site of irruption becomes covered with a coagulum of fibrin, and the tumultuous phenomena accordingly disappear; for the tubercles which are still in an early stage of their development are unable at that time to manufacture enough irritative material to cause well-marked symptoms to persist. But as the tubercles increase in size and as a fresh supply of toxins or bacilli is elaborated, either at the same or at some other site, a train of symptoms corresponding to the quantity of bacilli and of proteins is again inaugurated. The intervals of rest usually last only a few days; and if the patient happens to have several remissions at equal intervals, intermittent fever is simulated. Occasionally the period of improvement may last longer, until a renewed attack terminates life.

In one case of Reinhold's, for example, the woman was discharged feeling perfectly well after the first attack, and it was not until after an interval of almost a full month, during which not only fever but all other subjective symptoms were absent, that the disease reappeared insidiously and terminated the patient's life in three weeks (four months after the onset of the first symptoms). In a case of Henoch's the first attack, which lasted four days, was followed by an afebrile interval of well-being and increased strength lasting two months; this was followed by another attack, which lasted about six days, and, after an interval of twelve days, by another lasting five days.

Finally, after a few more days of freedom from symptoms the disease ended fatally at the end of five weeks.

Thus there may develop a chronic miliary tuberculosis which is not by any means to be sharply distinguished from the acute form and presents numerous transitional subvarieties. The symptoms of the latter are even more various and less definite.

The ultimate effect of associated bacteria on the development and course of acute miliary tuberculosis, the frequency and characteristic signs of such a mixed infection, remain to be explained by future clinical and pathologic investigation. But it is not improbable that the hemorrhages which have so frequently been observed are in part due to the presence of accidental bacteria (Babes).

DURATION.

The duration of acute miliary tuberculosis varies within wide limits, from a few hours to several months. One of the most fulminating cases was observed by Demme.

A girl five years of age, who, according "to the intelligent and observant parents," had not previously shown the slightest deviation from the normal, neither fever, loss of appetite, nor any change in disposition, was attacked by general convulsions while playing with other children, and died two and one-half hours later, the convulsions having continued without any interruption. The autopsy revealed widespread dissemination of miliary and submiliary tubercles in the pia mater, the lungs, pleura and peritoneum, as well as tuberculosis of the mesenteric glands.

A parallel case is that of Hager. A man, fifty-seven years of age, was admitted to the hospital for senile debility. Otherwise he felt perfectly well, and eight days later was still playing cards in the evening. The next day he was found dead in bed. Autopsy revealed general miliary tuberculosis of the lungs, liver, spleen, and kidneys.

These cases might be described as forms of miliary tuberculosis remaining ambulatory until death. It is rare, however, for death to appear so suddenly after the onset of the first symptoms. More frequently it happens that patients, especially such as suffer from marked cerebral phenomena, die from two to five or even ten days after they have first been forced to take to their beds. A case with a rapid course of this kind, culled from the records of the Prussian Military Hospitals, is reported by Grawitz, and is particularly noteworthy because up to the time of his admission to the hospital the man was performing his full military service. The case is as follows: An artillery man was taken to the hospital in a condition of complete collapse, loss of strength and consciousness, and died after four days. At the autopsy an old pulmonary tuberculosis and numerous recent miliary and submiliary tubercles in the lungs, pericardium, and pia mater were found.

Very mild prodromal symptoms, which are later recognized as having some relation to a miliary tuberculosis, may precede the disease by three or four months, and indicate a slight absorption of toxins.

The average duration of the usual severe form of the disease, with fever and the like, may be stated as two to three weeks, and for cases with only slight involvement of the brain from six to eight weeks. The duration obviously depends upon the character of the onset, the number of the bacilli and the quantity of the poison, the frequency of relapses, and the like. When the bacilli are few in number, the disease may be protracted from three to four months or longer.

Death is brought on by general exhaustion, cardiac weakness, dyspnea, and pulmonary edema. Sometimes the breathing stops quite suddenly; severe cyanosis develops, while the pulse continues to beat for a short time longer, but at a very irregular rate.

RECOVERY.

In very rare and exceptional cases acute miliary tuberculosis ends in complete recovery. The possibility of this occurrence has often been doubted, and many physicians still regard it as a chimera; but recovery from pulmonary phthisis was also for a long time doubted, although nowadays every one is convinced of its possibility, and striking examples of it are seen both at the autopsy table and in actual practice.

Waller as early as 1845 maintained that miliary tuberculosis was curable, and Wunderlich pointed out the frequent occurrence of tubercles even in very large numbers in cadavers, calling special attention to a case which recovered as a case of miliary tuberculosis and terminated fatally four months later from multiple capillary hemorrhages in the lungs, spleen, and kidney, and at the autopsy revealed the presence of old miliary tubercles. Sick also found in the lungs of a stone-mason, who had been hanged, in addition to emphysema a large number of nodules the size of a hempseed and extremely firm, feeling like cartilage, which, owing to the fact that they appeared to be all at the same stage of development, he regarded not as inspired particles of stone, but as the remains of a healed acute miliary tuberculosis. Burkart also reports from two autopsies on emphysematous subjects that the lungs were covered with small calcified and chalky white miliary tubercles which shone like mother-of-pearl.

Clinically, also, a number of cases have been observed that could be regarded as cases of recovery from acute miliary tuberculosis; but as the incurability was held as an axiom and no absolutely diagnostic signs of miliary tuberculosis were known before the discovery of the tubercle bacillus, cases of apparent recovery were never quite free from the objection that there might have been an error in diagnosis; and, as Wunderlich pointed out, it is not improbable that many a physician, who had been convinced that his diagnosis was well founded, when recovery later took place would begin to vacillate and ultimately upset his own diagnosis.

In view of these facts Sticker's observation is worth recording. He reports a case of severe miliary tuberculosis, proved to be such by repeated demonstration of tubercle bacilli in the blood, in which not only the bacilli disappeared—that might be explained in some other way—but in which improvement actually took place, although later the disease became converted into phthisis. Why should acute miliary tuberculosis be incurable, since tuberculous meningitis, which was formerly regarded as absolutely fatal, is curable, as some of the older observations suggest with a strong degree of probability (Dujardin-Beaumetz, Rilliet and Barthez, Schwalbe, and others) and the cases of Freyhan and Henkel indubitably prove?

Freyhan reports a case from the Fürbringer Hospital, in which the tuberculous nature of the meningitis was established beyond a doubt by the finding of tubercle bacilli in the cerebrospinal fluid obtained by puncture, and which nevertheless ended in recovery.

Henkel observed a boy ten years old with a tuberculous meningitis, in whom the diagnosis was also established by bacteriologic examination, and who recovered with some intellectual deficiency as the residuum of his disease.

Theoretically, there is no serious objection to the possibility of recovery from a miliary tuberculosis. Granted the possibility of a single tubercle becoming encapsulated, as has been abundantly proved, through inflammatory reaction produced by the proteins and undergoing absorption, it is difficult to see why the identical process should not take place in 100 or 1000 or even more independent nodules. The toxins, although they produce such tumultuous symptoms, are not retained in the body, but undergo chemical changes and are then excreted. In my opinion, a patient with miliary tuberculosis is much less exposed to the danger that the many thousands of tubercles may fail to heal, than to the danger of renewed infection from the old blood-vessel focus or some other rupture, and the resultant intoxication before a spontaneous recovery can take place in the ordinary way.

Such improvement must necessarily be entremely gradual. According to Wunderlich, who, as has been previously mentioned, was a strong advocate of the curability of the disease, it requires at least from six to eleven weeks; but in any case the physician must be prepared to see his hopes destroyed by a renewed, more severe irruption of bacilli or by conversion into phthisis.

CHAPTER V.

DIAGNOSIS AND PROGNOSIS.

DIAGNOSIS.

The diagnosis of acute general miliary tuberculosis is often attended by considerable difficulties, for we are practically without any means of establishing the diagnosis with absolute certainty. The only thing that meets every requirement is the demonstration of **tubercle bacilli in the blood.** Weichselbaum and Rütimeyer have found tubercle bacilli post mortem in blood-clots from the heart; and Rütimeyer, Lustig, Sticker, Ulacacis, and Doutrelepont during life in the blood in cases of acute miliary tuberculosis.

In making the examination after Lustig's method, the tip of the finger is thoroughly cleansed and pricked with a needle and the blood drawn out through a capillary tube, or, after Weichselbaum's suggestion, a cup may be applied in order to obtain more blood. The blood may, if necessary, be diluted, sedimented, and centrifuged. Animal experiments and the usual culture procedures take too much time and are always unsuitable because a rapid decision is of the greatest necessity in such cases. Whether the culture-medium suggested by Hesse will yield satisfactory results remains to be decided by future experiments.

The procedure recommended by a certain author, to withdraw blood directly from the spleen by puncture, I do not regard as permissible during life, even if it promised to yield better results; for the "somewhat gaping, linear tears in the capsule, about 0.5 cm. in length," found post mortem in the spleen in such cases, the "bloody fibrinous deposits" at the site of puncture in the spleen, and the finding of "about two tablespoonfuls of dark fluid blood in the abdominal cavity opposite the site of puncture"—clearly prove that an interference of this kind may, under certain circumstances, hasten propagation of the disease, if it is performed not, as by the author in question, immediately before death, but at a time when the diagnosis would still be of some practical importance.

While the positive demonstration of bacilli in the blood is extremely valuable, too much must not be expected from the practical working of this method. Even in examinations of cadavers Weichselbaum examined 9 preparations before he succeeded in finding 2 bacilli; Meisels found one bacillus in each of 2 out of 18 preparations; and in the living subject Lustig succeeded in finding only a few bacilli in 30 to 40 preparations, while Rütimeyer once failed to find a single bacillus in 20 preparations. Hence a positive finding *intra vitam* always presupposes a laborious and time-consuming search, and the examiner must take great care to avoid mistaking the hemin crystals for tubercle bacilli, which they greatly resemble (Lustig and Rütimeyer). Whether or not the examiner happens to make his examination at a suitable time after rupture has taken place will often depend upon a lucky accident; for even in miliary tuberculosis the bacilli do not, as many authors seem to think, circulate constantly in the blood, being at once deposited again after rupture has taken place. Wyssokowitsch's experiments showed that bacteria introduced into the circulation, when they are such as cannot develop in the blood, disappear again after a few hours; it is probable, however, that tubercle bacilli, owing to their small size, succeed in holding their ground somewhat longer.

As a matter of fact, the demonstration of bacilli in the blood, to judge from the few communications in regard to the method to be found in the literature (Kroenig and others), appears to enjoy but little favor among physicians.

If marked meningitic phenomena form a part of the clinical picture, a second means of determining the diagnosis will be found in the attempt to demonstrate the presence of **tubercle bacilli in the cerebrospinal fluid,** as was first done by Lichtheim, Fürbringer, and Dennig. A positive result in this respect clears up not only the character of the meningitis, but also that of the general disease.

A third but somewhat unreliable procedure is the demonstration of **choroidal tubercles.** Here, again, certain restrictions must be borne in mind. In the first place, the bacilli are not always poured into the blood in such abundance as to involve all the organs, including the choroid. In other words, a widespread miliary tuberculosis may exist and even the meninges may be attacked, while the choroid coat of the eye nevertheless escapes. If the result of the examination is positive, it is true that a general miliary tuberculosis may be inferred with a very great degree of certainty; for cases of choroidal tuberculosis in the absence of general miliary tuberculosis are very rare exceptions, and from a practical standpoint, so far as prognosis, etc., is concerned, they cannot be separated from general tuberculosis.

Miliary tubercles in the pharynx, larynx, and in the accessible mucous membranes generally, may also assist in clearing up the diagnosis.

All these examinations, especially the inspection of the choroid, must be repeated every twelve to twenty-four hours, because the tubercles do not become visible until they have attained a certain size, and experience has shown that in areas which at first exhibited no changes small tubercles may make their appearance twelve to twenty-four hours later. It is to be remembered that at least one to two weeks must elapse after the rupture and escape of the tubercle bacilli before they attain a size of 0.5 mm., which is necessary for perception with the naked eye.

The sputum yields no information that can be utilized for the diagnosis of miliary tuberculosis, because tubercle bacilli are not liberated unless the tubercles break down and perforation takes place into an open bronchus. Their occurrence, therefore, would only indicate an old focus, unless it should accidentally be the case that the miliary tubercles derived from a former irruption were already in a state of degeneration.

Tubercle bacilli in the urine and in the stools also are indications merely of the existence of old foci and only indirectly valuable for the diagnosis.

If the above enumerated, fairly reliable signs are absent, the diagnosis must be based on the history and the grouping of the clinical symptoms.

DIFFERENTIATION FROM TYPHOID FEVER.

The greatest danger lies in confounding an example of the typhoidal form with typhoid fever. The history alone affords valuable hints for this distinction. In the first place, it is to be remembered that, although fever is the rule, an afebrile course is not an argument against miliary tuberculosis. In favor of typhoid fever we have the demonstration of a typhoid epidemic or at least of several cases of typhoid fever in the immediate or more remote neighborhood of the patient, and the history of his having come in contact with such patients; in favor of miliary tuberculosis, especially in children, a tuberculous family history, and in the case of older persons the history of tuberculosis among business associates. The external appearance of the patient, the characteristic signs of tuberculosis or scrofulosis, may be guardedly utilized in favor of miliary tuberculosis, although even the most blooming appearance must not be allowed to preclude the diagnosis of miliary tuberculosis. The demonstration of an old tuberculous focus of apical disease, or some affection of the glands or bones; tuberculous middle-ear catarrh; a former hemoptysis or pleurisy, or the occurrence immediately preceding the attack in question of pleurisy with effusion and rapid absorption, as in Litten's cases, especially when its tuberculous nature has been established; rapidly diminishing cervical glands; cough of long standing; frequent attacks of dyspnea; a history of measles (or whooping-cough) at no distant date; and the puerperium may arouse a suspicion of miliary tuberculosis—in the last-mentioned cases especially if cough existed during pregnancy and fever occurred a short time after delivery. Typhoid fever is characterized by the demonstration of typhoid bacilli in the blood, in the rose spots, in the urine, and especially in the feces (Piorkowski's medium!); and, above all, by the Gruber-Widal serum diagnosis. [For other details see treatises upon this subject.]

As regards the actual symptoms of the disease, the fever when not influenced by medication is, as a rule, not so high in an ordinary case of miliary tuberculosis nor so continuous as in typhoid fever. The changeable character of the fever, the great irregularity in the occurrence of the acme, or the great variability in the time of maximum temperature on different days, and more than anything else the *inverse type*, point to miliary tuberculosis. Such irregularities are rare in typhoid fever and occur only under unusual circumstances, such as old age, after an antecedent severe disease, etc. (Wunderlich).

Marked acceleration of the breathing and later severe dyspnea, without any physically demonstrable causes proportionate to the degree of disturbance, point to miliary tuberculosis. Similarly, the extreme frequency of the pulse-rate, which greatly exceeds the level proportional to the corresponding height of the temperature, is a peculiarity of miliary tuberculosis but a rare occurrence in typhoid fever. A soft pulse is also more common in miliary tuberculosis, while dicrotism in general, especially persistent dicrotism, is especially observed in typhoid fever.

In miliary tuberculosis the cough is more severe and distressing to the patient; the bronchial symptoms are more intense and develop earlier, while in typhoid fever they do not, as a rule, appear before the end of the first week or later. Jürgensen's friction murmurs and pleuritic symptoms in general have some weight in favor of miliary tuberculosis.

If there is little or no meteorism, no pain or gurgling in the ileocecal region, at least no characteristic pea-soup stools with the peculiar stratification; if the spleen enlarges slowly or the enlargement is only slight; if the organ is barely palpable—all these factors are strongly in favor of miliary tuberculosis, although it is true that in typhoid fever intestinal symptoms are sometimes wanting and the splenic enlargement, especially in old individuals with rigid capsule, is but little marked. The typhoid spleen is usually somewhat harder than that of tuberculosis.

Pallor and cyanosis of the skin, herpes, and well-marked *taches cérébrales* may be mentioned as comparatively frequent signs in miliary tuberculosis; while roseola is a symptom of extreme rarity. Roseola always speaks more or less for typhoid fever, and in direct proportion to the distinctness of its development. On the other hand, the absence of rose spots just as little precludes typhoid altogether as their presence precludes that of miliary tuberculosis.

Copious hemorrhages from the mouth and nose are very rare in acute miliary tuberculosis; they were observed by Jacubasch-Henoch and by Senator. Their occurrence, however, is more in favor of typhoid fever. Early cardiac debility and rapid progressive loss of strength also, as a rule, point to miliary tuberculosis.

Parotitis is rare in miliary tuberculosis (one case by Stabel, Senator), but fairly common in typhoid fever.

The assertion that violent delirium and loud talking are usually absent in tuberculosis, and that profuse sweats and unusually heavy urinary sediments are points against typhoid fever, is worthy of but little credence.

No one of these signs is in itself decisive; they all have to be carefully weighed in the hope of finding in their combination a more or less decisive indication in favor of either miliary tuberculosis or typhoid fever. The diagnosis is especially difficult or impossible when the physician has not had an opportunity of tracing the development of the disease himself because the patient is not treated until late. During the subsequent course of the disease a rapid improvement argues against tuberculosis. Occasionally the symptoms of miliary tuberculosis are so completely identical with those which occur in typhoid fever that a distinction is quite impossible. Such a case was reported by Senator; the enlargement of the spleen, distinct roseola, epistaxis, dicrotism of the pulse, singultus, difficult hearing, suppurative parotitis, and a series of other symptoms absolutely characterized the case as one of typhoid fever, and misled even the expert diagnostician, although the case at the autopsy revealed itself as one of miliary tuberculosis. Similar observations are reported by Eichhorst, Hager, and de Bruice. In the last-mentioned case, which was attended also by hematuria, copious epistaxis, hemorrhages from the gums, and ecchymoses in addition to a roseola, splenic enlargement, liquid stools, and typhoid type of fever, ophthalmoscopic examination revealed the presence of choroidal tubercles. The mistake is sometimes absolutely unavoidable; for it is well known that typhoid fever frequently runs a very atypical course, the rose spots may be very faint and the diarrhea quite uncharacteristic.

The problem may be peculiarly complicated when the miliary tuberculosis develops during the height of the typhoid fever, or immediately follows the termination of that disease (Birch-Hirschfeld, Burkart, Massini, Schütz), in opposition to the view which was formerly widely entertained, that typhoid fever and tuberculosis mutually exclude each other and which suffered its first blow when Cless reported his observation of the combination between pulmonary tuberculosis and typhoid fever. In such cases it may be quite impossible to recognize the true state of affairs, and a decision may not be arrived at during life, especially as the transition to miliary tuberculosis is attended by approximately the same symptoms as the antecedent typhoidal disease, so that the physician is at first inclined to think of a relapse.

DIFFERENTIATION FROM EMPHYSEMA, ETC.

It was formerly believed, also chiefly on Rokitansky's authority, that inveterate **emphysema** also possessed the peculiarity of excluding tuberculosis. Cless first restricted this proposition in its application to the most severe grades of emphysema, and later Wunderlich's and Burkart's observations finally proved that the association of acute miliary tuberculosis with severe emphysema is not infrequent. Among 18 cases of acute miliary tuberculosis Burkart found 12 associated with severe emphysema—a high percentage which is probably accidental. It is in cases of inveterate emphysema and bronchitis, with degeneration of the heart, that the correct diagnosis may present the greatest difficulties, as in the cases reported by Litten, Görne, Hager, and Heitler.

It is true that rapid loss of strength, emaciation, great frequency of the respiration and protracted dry catarrh, with early cerebral symptoms and splenic tumor, are points in favor of miliary tuberculosis; but, on the one hand, there are cases of diffuse **capillary bronchitis** which may exhibit a severe involvement of the cerebrum—headache going on to apathy, somnolence, delirium and even convulsions—with other symptoms usually peculiar to miliary tuberculosis, such as fever up to 40° C. (104° F.), chills, cyanosis, and the like. Again, cases occur in old persons that, so far as intensity and the nature of the symptoms are concerned, fall little short of an acute miliary tuberculosis. On the other hand, miliary tuberculosis, especially in old persons (for example, Burkart's, Leichtenstern's, and Hager's cases), often runs such a comparatively mild course, with faintly marked fever or without any fever whatever, as to be regarded merely as a change for the worse of the already existing bronchitis.

The occurrence of rusty brown sputum or the onset of fever with chill and the finding of dulness on percussion have sometimes simulated a croupous pneumonia, as, for example, in Hager's cases. In the main, however, the fact that the signs of infiltration are less pronounced and the less typical course of the fever will usually enable one to make the distinction.

If by chance the successive invasions of the poison in miliary tuberculosis should by some accident take place at fairly regular intervals, the picture of an intermittent fever would be produced. Aside from the history of **malaria,** the nature of the splenic enlargement, the rapid effect of quinin medication, the absence of bronchitic phenomena are points in favor of malaria; while a lesser degree of pyrexia with regularity of the fever, a subnormal apyrexia or the prominence of bronchitic symptoms and rapid loss of flesh and strength would be in favor of miliary tuberculosis.

In **pregnant women** so-called uncontrollable vomiting may usher in an acute miliary tuberculosis, or dyspnea going on to fatal asphyxia may be the only symptom. Excessively rapid loss of weight may under certain circumstances determine the diagnosis.

Pyemia and **septicemia,** after purulent phlebitis of the sinuses in the brain or the internal jugular, for example, or secondary to an otitis, may also present at times a symptomatic resemblance to miliary tuberculosis. The character of the underlying otitis will be of some importance in the diagnosis.

Miliary tuberculosis, when it begins with violent delirium, may also be confounded with **acute mania.**

In a case of Reinhold's the disease for weeks presented the picture of a typical erythema nodosum with moderate fever and rheumatoid symptoms, until finally meningitic symptoms developed. The disease, finally, may be masked by tuberculous pericarditis or peritonitis; less frequently, however, than by meningitis.

PROGNOSIS.

It follows from what has been said that the prognosis is extremely bad, in fact, practically fatal; but the fact that it is not absolutely fatal is of some importance. Even for the patient it is some gain that the physician does not come to his bedside with a paralyzing sense of complete hopelessness, but rather with the conviction that recovery is not absolutely precluded and that there remains to him only the sad task of at least providing for euthanasia. The importance of this fact and its influence not only on the psychic condition of a patient who retains his consciousness, but also on the physician's acts, is not to be underestimated.

It is true that we do not have it in our power to prevent an irruption or a relapse of the disease; but when the needle on the balance swings to and fro, it is possible, by guarding the patient against every conceivable source of injury and by carefully maintaining his strength, to turn the scale in favor of a successful termination. The improvement that occasionally takes place, although it is true only temporarily, even when the exhaustion is extreme, the temperature very high, and the patient completely unconscious, shows that the vital force has not been exhausted by the initial onslaught of the disease. When the heart is vigorous, the disease may be resisted for some time, especially if it is due chiefly to the absorption of toxins. If the body has been weakened by other antecedent diseases and the heart has suffered from age and the vicissitudes of life, and if, the body having been overwhelmed by poison during an antecedent phthisis, the relapses are frequent and intense, death is to be more certainly and more rapidly expected.

CHAPTER VI.

PROPHYLAXIS AND TREATMENT.

The only rational prophylaxis of miliary tuberculosis coincides with the prophylaxis of tuberculosis in general, *i. e.*, it consists in preventing a primary infection, a primary tuberculous focus which may later become the starting-point of an acute miliary tuberculosis. The precautions to be observed in this respect have been described in detail in the section on Tuberculosis.

If there already exists a demonstrable focus somewhere in the body, its earliest possible healing through encapsulation is indicated for prophylactic reasons, and there is reason to believe that such an event can be materially hastened by strengthening the body, and by insisting on abundant nutritious diet and the exact observance of hygienic rules. The position of the focus may be such that early removal by surgical means will be the most radical prophylactic measure.

The treatment of acute miliary tuberculosis at the present time is unfortunately a very thankless task. Beyond the effort to keep up the strength as much as possible and, by providing favorable hygienic conditions, to guard against any possible injury in order to preserve life as long as possible and, in case the relapses cease and the miliary tubercles become obliterated, to assure a favorable termination, there is practically nothing to be done except to meet the symptoms. Stimulants are, in the first place, indicated to increase the strength of the heart and perhaps to bridge over the most trying time of the acute irruptions. Camphor and invigorating wines are therefore indicated, and narcotics may be required when violent symptoms, cough, or insomnia predominate and threaten to consume the patient's strength. If the temperature is excessive, cool baths and, in rare cases, the antipyretics, antifebrin, lactophenin, and the like, with warm moist compresses to allay the pain, may be indicated.

Potassium iodid has been recommended at various times, and Janssen reports a case of tuberculous meningitis in an adult which was treated with large doses of potassium iodid (8 grams a day, increased within a few days to 40 grams), the patient receiving altogether 950 grams, and was thereby (or in spite of that treatment?) cured. When the cerebral symptoms are very severe, partial removal of the cerebrospinal fluid may under certain circumstances be considered for the purpose of reducing the cerebral pressure and making the patient's death less painful to him and for those about him.

ABBREVIATIONS USED IN THE BIBLIOGRAPHY.

Ac. d. sc.	Académie des sciences.
Aerztl. I. Bl.	Aerztliche internationale Blätter.
A. M. C. Z.	Allgemeine medicinische Centralzeitung.
A. J.	American Journal.
Ann. Past.	Annales de l'Institut Pasteur.
Ann.	Annales.
Arb. Kais. G. A.	Arbeiten aus dem Kaiserlichen Gesundheitsamt.
Arb.	Arbeiten.
A. f. D.	Archiv für Dermatologie und Syphilis.
A. f. exp. Path. u. Pharm.	Archiv für experimentelle Pathologie und Pharmakologie.
A. d. Heilk.	Archiv der Heilkunde.
A. f. H.	Archiv für Hygiene.
A. f. Khlk.	Archiv für Kinderheilkunde.
A. f. kl. Ch.	Archiv für klinische Chirurgie.
A. f. L.	Archiv für Laryngologie und Rhinologie.
A. f. O.	Archiv für Ohrenheilkunde.
A. de. m. exp.	Archiv de médecine expérimentale et de l'anatomie pathologique.
A. d. Phys.	Archive de Physiologie.
Arch. per sc. m.	Archiv per le science médicale.
Bd.	Band = Volume.
Ziegler's Beitr.	Beiträge zur pathologischen Anatomie und Physiologie.
Br.	Bericht = Report.
B. kl. W.	Berliner klinische Wochenschrift.
Br. M. J.	British Medical Journal.
Btr. z. kl. Ch.	Brun's Beiträge zur klinischen Chirurgie.
Bull. de l'Ac.	Bulletin de l'Académie.
Ch. A.	Charité-Annalen.
C. f. allg. Gespfl.	Centralblatt für allgemeine Gesundheitspflege.
C. f. a. Path.	Centralblatt für allgemeine Pathologie und pathologische Anatomie.
C. f. B.	Centralblatt für Bakteriologie und Parasitenkunde.
C. f. Ch.	Centralblatt für Chirurgie.
C. f. kl. M.	Centralblatt für klinische (resp. innere) Medicin.
C. f. L.	Centralblatt für Laryngologie.
C. f. m. W.	Centralblatt für die medicinischen Wissenschaften.
C. f. Aughlk.	Centralblatt für praktische Augenheilkunde.
C. r.	Comptes-rendus.
Cgr.	Congress.
Cor. f. Sch. Ae.	Correspondenzblatt für Schweizer Aerzte.
Cor.	Correspondenzblatt.
A. f. kl. M.	Deutsches Archiv für klinische Medicin.
D. M. Z.	Deutsche Medicinalzeitung.
D. m. W.	Deutsche medicinische Wochenschrift.
D. mil.-ä. Z.	Deutsche militärärztliche Zeitschrift.
Z. f. Thierm.	Deutsche Zeitschrift für Thiermedicin und vergleichende Pathologie.
Estr.	Estrato.
F. d. M.	Fortschritte der Medicin.
Gz. hebd.	Gazette hebdomadaire de méd. et chir. de Paris.

Gz. des hôp.	Gazette des hôpitaux.
Gz.	Gazette.
A. f. Oph.	v. Gräfe's Archiv für Ophthalmologie.
H.	Heft = Number.
Hyg. R.	Hygienische Rundschau.
Jb.	Jahrbuch.
Jbr.	Jahresbericht.
In.-Diss.	Inauguraldissertation.
J.	Journal.
Lanc.	The Lancet.
Lang. A.	Langenbeck's Archiv.
M. Jb.	Medicinische Jahrbücher.
M. Kais. G. A.	Mittheilungen aus dem Kaiserlichen Gesundheitsamt.
Mh. f. pr. D.	Monatshefte für praktische Dermatologie.
Mschr. f. O.	Monatsschrift für Ohrenheilkunde.
M. m. W.	Münchener medicinische Wochenschrift.
p.	pagina = page.
Pet. m. W.	Petersburger medicinische Wochenschrift.
Pr. m. W.	Prager medicinische Wochenschrift.
R. de hyg.	Revue de hygiène.
R. de m.	Revue de médecine.
R.	Revue.
Schmidt's Jb.	Schmidt's Jahrbücher.
S. m.	La Semaine médicale.
Sitz. Ber.	Sitzungsbericht.
Soc.	Société.
Th. de Paris.	Thèse de Paris.
t.	tome = volume.
Un. m.	L'Union médical.
Vh.	Verhandlung.
Vers.	Versammlungen.
Vj. f. D.	Vierteljahrsschrift für Dermatologie und Syphilis.
V. A.	Virchow's Archiv.
W. kl. W.	Wiener klinische Wochenschrift.
W. m. Pr.	Wiener medicinische Presse.
W. m. W.	Wiener medicinische Wochenschrift.
Kl., M. f. Aughlk.	Zehender's klinische Monatsblätter für Augenheilkunde
Z. f. Biol.	Zeitschrift für Biologie.
Z. f. Ch.	Zeitschrift für Chirurgie.
Z. f. H.	Zeitschrift für Hygiene und Infectionskrankheiten.
Z. f. kl. M.	Zeitschrift für klinische Medicin.
Z. f. O.	Zeitschrift für Ohrenheilkunde.
Z. f. w. M.	Zeitschrift für wissenschaftliche Mikroskopie.

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